```
FILE 'REGISTRY' ENTERED AT 12:05:04 ON 11 APR 2001
L1             1 S FORMESTANE/CN
L2          1477 S ANDROST-4-ENE-3,17-DIONE
L3             0 S ANDROST-4-ENE-3,17-DIONE (W) 4-ACETOXY
L4            22 S ANDROST-4-ENE-3,17-DIONE (W) 4-ACETYLOXY
L5             0 S ANDROST-4-ENE-3,17-DIONE, 4-ACETYLOXY/CN
L6               STRUCTURE UPLOADED
L7             0 S L6
L8             0 S L6 FULL
L9               STRUCTURE UPLOADED
L10            0 S L9
L11              STRUCTURE UPLOADED
L12            2 S L11
L13            0 S L11 EXA
L14            1 S L11 EXA FULL

     FILE 'CAPLUS, MEDLINE, USPATFULL, BIOSIS, EMBASE' ENTERED AT 12:58:13 ON
     11 APR 2001
L15         1414 S L1 OR L14 OR FORMESTANE
L16       203235 S TOPICAL
L17      1564492 S CREAM OR OINTMENT OR GEL OR EMULS?
L18           20 S L17 AND L15
L19           19 DUPLICATE REMOVE L18 (1 DUPLICATE REMOVED)
L20         5112 S PENETRAT? (W) (PROMOT? OR ENHANC?)
L21            2 S L20 AND L19

     FILE 'REGISTRY' ENTERED AT 13:50:27 ON 11 APR 2001
L22            1 S DMSO/CN

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS, USPATFULL' ENTERED AT 13:51:15 ON
     11 APR 2001
L23       139466 S L22 OR DMSO OR DIMETHYL SULFOXIDE

=> s l15 and l23
L24            7 L15 AND L23
```

```
  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:04:55 ON 11 APR 2001

=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.15       0.15

FILE 'REGISTRY' ENTERED AT 12:05:04 ON 11 APR 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES:   10 APR 2001  HIGHEST RN 330783-20-5
DICTIONARY FILE UPDATES:  10 APR 2001  HIGHEST RN 330783-20-5

TSCA INFORMATION NOW CURRENT THROUGH July 8, 2000

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Structure search limits have been increased.  See HELP SLIMIT
for details.

=> s formestane/cn
L1            1 FORMESTANE/CN

=> d

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN   566-48-3  REGISTRY
CN   Androst-4-ene-3,17-dione, 4-hydroxy- (8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   4-HAD
CN   4-Hydroxyandrost-4-ene-3,17-dione
CN   4-Hydroxyandrostene-3,17-dione
CN   4-Hydroxyandrostenedione
CN   4-OHA
CN   CGP 32349
CN   CRC 82/01
CN   Formestane
CN   Lentaron
FS   STEREOSEARCH
DR   127128-20-5
MF   C19 H26 O3
LC   STN Files:   ADISINSIGHT, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS,
       BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS,
       CHEMINFORMRX, CIN, CSCHEM, DDFU, DRUGNL, DRUGU, DRUGUPDATES, EMBASE,
       IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, SYNTHLINE, TOXLINE, TOXLIT,
       USAN, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   WHO

Absolute stereochemistry.
```
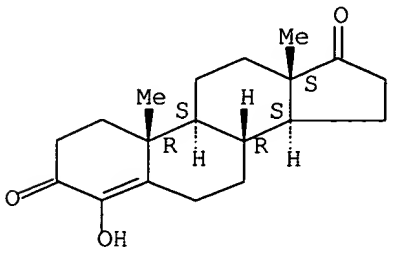




```
          244 REFERENCES IN FILE CA (1967 TO DATE)
            4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
```

244 REFERENCES IN FILE CAPLUS (1967 TO DATE)

```
=> log h
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         5.61       5.76

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 12:05:38 ON 11 APR 2001
Trying 3106016892...Open

Welcome to STN International!  Enter x:x
LOGINID:ssspta1617srh
PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'REGISTRY' AT 12:43:23 ON 11 APR 2001
FILE 'REGISTRY' ENTERED AT 12:43:23 ON 11 APR 2001
COPYRIGHT (C) 2001 American Chemical Society (ACS)

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         5.61       5.76

=> s androst-4-ene-3,17-dione
         27376 ANDROST
       9855213 4
       2598941 ENE
          3638 ENES
       2598941 ENE
                  (ENE OR ENES)
         19867 3,17
        594830 DIONE
             1 DIONES
        594830 DIONE
                  (DIONE OR DIONES)
L2        1477 ANDROST-4-ENE-3,17-DIONE
                  (ANDROST(W)4(W)ENE(W)3,17(W)DIONE)

=> s androst-4-ene-3,17-dione (w) 4-acetoxy
         27376 ANDROST
       9855213 4
       2598941 ENE
          3638 ENES
       2598941 ENE
                  (ENE OR ENES)
         19867 3,17
        594830 DIONE
             1 DIONES
        594830 DIONE
                  (DIONE OR DIONES)
          1477 ANDROST-4-ENE-3,17-DIONE
                  (ANDROST(W)4(W)ENE(W)3,17(W)DIONE)
       9855213 4
         15069 ACETOXY
          1452 4-ACETOXY
                  (4(W)ACETOXY)
L3           0 ANDROST-4-ENE-3,17-DIONE (W) 4-ACETOXY

=> s androst-4-ene-3,17-dione (w) 4-acetyloxy
         27376 ANDROST
       9855213 4
       2598941 ENE
          3638 ENES
       2598941 ENE
                  (ENE OR ENES)
         19867 3,17
        594830 DIONE
             1 DIONES
        594830 DIONE
                  (DIONE OR DIONES)
          1477 ANDROST-4-ENE-3,17-DIONE
                  (ANDROST(W)4(W)ENE(W)3,17(W)DIONE)
       9855213 4
```

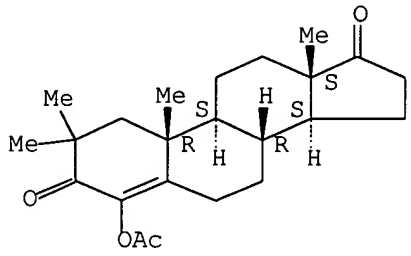
220306 ACETYLOXY
28213 4-ACETYLOXY
(4(W)ACETYLOXY)
L4 22 ANDROST-4-ENE-3,17-DIONE (W) 4-ACETYLOXY

=> d1-5
D1-5 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d 1-5

L4 ANSWER 1 OF 22 REGISTRY COPYRIGHT 2001 ACS
RN 132609-69-9 REGISTRY
CN **Androst-4-ene-3,17-dione, 4-(acetyloxy)-2,2-dimethyl- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H32 O4
SR CA
LC STN Files: CA, CAPLUS

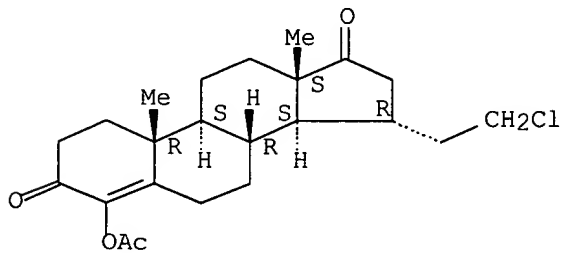
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L4 ANSWER 2 OF 22 REGISTRY COPYRIGHT 2001 ACS
RN 119190-15-7 REGISTRY
CN **Androst-4-ene-3,17-dione, 4-(acetyloxy)-15-(2-chloroethyl)-, (15.alpha.)- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H31 Cl O4
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

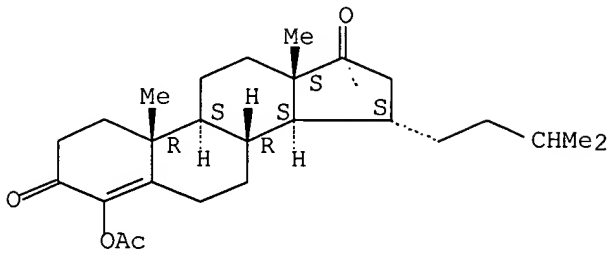


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L4 ANSWER 3 OF 22 REGISTRY COPYRIGHT 2001 ACS
RN 119164-88-4 REGISTRY
CN **Androst-4-ene-3,17-dione, 4-(acetyloxy)-15-(3-methylbutyl)-, (15.alpha.)- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH

MF C26 H38 O4
SR CA
LC STN Files: CA, CAPLUS

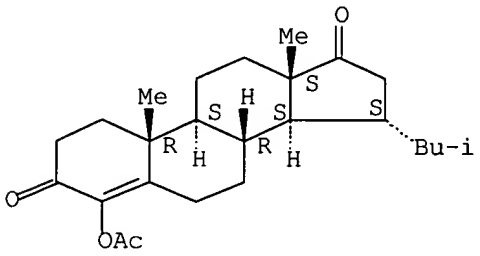
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L4 ANSWER 4 OF 22 REGISTRY COPYRIGHT 2001 ACS
RN 119164-87-3 REGISTRY
CN **Androst-4-ene-3,17-dione, 4-(acetyloxy)-15-(2-methylpropyl)-, (15.alpha.)- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF C25 H36 O4
SR CA
LC STN Files: CA, CAPLUS

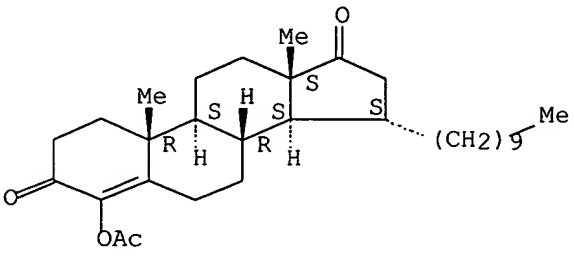
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L4 ANSWER 5 OF 22 REGISTRY COPYRIGHT 2001 ACS
RN 119164-86-2 REGISTRY
CN **Androst-4-ene-3,17-dione, 4-(acetyloxy)-15-decyl-, (15.alpha.)- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H48 O4
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



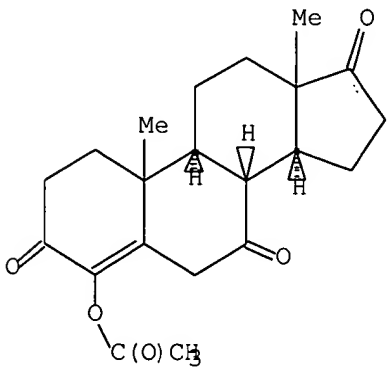
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> s androst-4-ene-3,17-dione, 4-acetyloxy/cn
L5 0 ANDROST-4-ENE-3,17-DIONE, 4-ACETYLOXY/CN

=>
Uploading 09646355.str

L6 STRUCTURE UPLOADED

=> d
L6 HAS NO ANSWERS
L6 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l6
SAMPLE SEARCH INITIATED 12:51:26 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 995 TO ITERATE

100.0% PROCESSED 995 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 18008 TO 21792
PROJECTED ANSWERS: 0 TO 0

L7 0 SEA SSS SAM L6

=> s l6 full
FULL SEARCH INITIATED 12:51:44 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 19657 TO ITERATE

100.0% PROCESSED 19657 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.02

L8 0 SEA SSS FUL L6

=> log h
COST IN U.S. DOLLARS SINCE FILE ENTRY 225.46 TOTAL SESSION 225.61
FULL ESTIMATED COST

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 12:52:14 ON 11 APR 2001
Connection closed by remote host

Trying 3106016892...Open

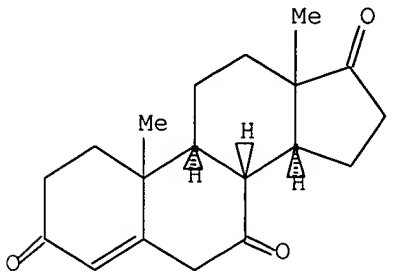
Welcome to STN International! Enter x:x
LOGINID:ssspta1617srh
PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'REGISTRY' AT 12:53:51 ON 11 APR 2001
FILE 'REGISTRY' ENTERED AT 12:53:51 ON 11 APR 2001
COPYRIGHT (C) 2001 American Chemical Society (ACS)

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	225.46	225.61

=>
Uploading 9646355a.str

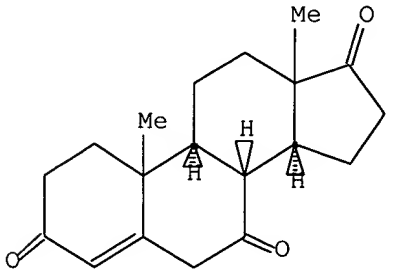
L9   STRUCTURE UPLOADED

=> d
L9 HAS NO ANSWERS
L9   STR



Structure attributes must be viewed using STN Express query preparation.

=> d 19
L9 HAS NO ANSWERS
L9   STR



Structure attributes must be viewed using STN Express query preparation.

=> s 19
SAMPLE SEARCH INITIATED 12:54:44 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   8983 TO ITERATE

 11.1% PROCESSED   1000 ITERATIONS   0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:	ONLINE	**COMPLETE**
	BATCH	**COMPLETE**
PROJECTED ITERATIONS:	173990 TO	185330
PROJECTED ANSWERS:	0 TO	0

L10 0 SEA SSS SAM L9

=>
Uploading 09646355.str

L11 STRUCTURE UPLOADED

=>`s l11
SAMPLE SEARCH INITIATED 12:56:05 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1183 TO ITERATE

84.5% PROCESSED 1000 ITERATIONS 2 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

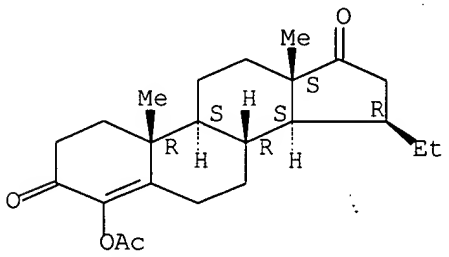
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 21598 TO 25722
PROJECTED ANSWERS: 2 TO 139

L12 2 SEA SSS SAM L11

=> d tot

L12 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2001 ACS
RN 119164-69-1 REGISTRY
CN Androst-4-ene-3,17-dione, 4-(acetyloxy)-15-ethyl-, (15.beta.)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H32 O4
SR CA
LC STN Files: CA, CAPLUS

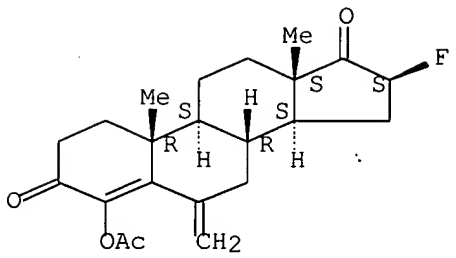
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

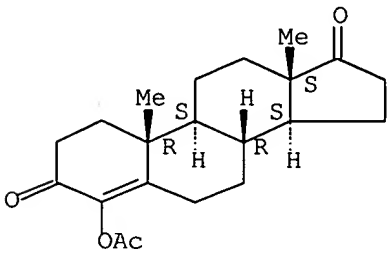
L12 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2001 ACS
RN 115836-75-4 REGISTRY
CN Androst-4-ene-3,17-dione, 4-(acetyloxy)-16-fluoro-6-methylene-, (16.beta.)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H27 F O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

```
=> s l11 exa
SAMPLE SEARCH INITIATED 12:56:33 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     11 TO ITERATE

100.0% PROCESSED      11 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           22 TO      418
PROJECTED ANSWERS:               0 TO        0

L13           0 SEA EXA SAM L11

=> s l11 exa full
FULL SEARCH INITIATED 12:56:43 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    259 TO ITERATE

100.0% PROCESSED     259 ITERATIONS                               1 ANSWERS
SEARCH TIME: 00.00.01

L14           1 SEA EXA FUL L11

=> d

L14  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN   61630-32-8  REGISTRY
CN   Androst-4-ene-3,17-dione, 4-(acetyloxy)- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   4-Acetoxy-4-androstene-3,17-dione
FS   STEREOSEARCH
MF   C21 H28 O4
LC   STN Files:   BEILSTEIN*, BIOSIS, CA, CANCERLIT, CAPLUS, CHEMCATS, CSCHEM,
       EMBASE, MEDLINE, RTECS*, TOXLINE, TOXLIT, USPATFULL
         (*File contains numerically searchable property data)

Absolute stereochemistry.
```



23 REFERENCES IN FILE CA (1967 TO DATE)
23 REFERENCES IN FILE CAPLUS (1967 TO DATE)

```
=> file caplus medline mbase biosis
'MBASE' IS NOT A VALID FILE NAME
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available.  If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.
ENTER A FILE NAME OR (IGNORE):uspatfull, embase
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     276.88     277.03

FILE 'CAPLUS' ENTERED AT 12:58:13 ON 11 APR 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 12:58:13 ON 11 APR 2001

FILE 'USPATFULL' ENTERED AT 12:58:13 ON 11 APR 2001
CA INDEXING COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 12:58:13 ON 11 APR 2001
COPYRIGHT (C) 2001 BIOSIS(R)

FILE 'EMBASE' ENTERED AT 12:58:13 ON 11 APR 2001
COPYRIGHT (C) 2001 Elsevier Science B.V.  All rights reserved.

=> d his

     (FILE 'HOME' ENTERED AT 12:04:55 ON 11 APR 2001)

     FILE 'REGISTRY' ENTERED AT 12:05:04 ON 11 APR 2001
L1             1 S FORMESTANE/CN
L2          1477 S ANDROST-4-ENE-3,17-DIONE
L3             0 S ANDROST-4-ENE-3,17-DIONE (W) 4-ACETOXY
L4            22 S ANDROST-4-ENE-3,17-DIONE (W) 4-ACETYLOXY
L5             0 S ANDROST-4-ENE-3,17-DIONE, 4-ACETYLOXY/CN
L6               STRUCTURE UPLOADED
L7             0 S L6
L8             0 S L6 FULL
L9               STRUCTURE UPLOADED
L10            0 S L9
L11              STRUCTURE UPLOADED
L12            2 S L11
L13            0 S L11 EXA
L14            1 S L11 EXA FULL

     FILE 'CAPLUS, MEDLINE, USPATFULL, BIOSIS, EMBASE' ENTERED AT 12:58:13 ON
     11 APR 2001

=> s l1 or l14 or formestane
L15         1414 L1 OR L14 OR FORMESTANE

=> s topical
L16       203235 TOPICAL

=> s cream or ointment or gel or emuls?
L17      1564492 CREAM OR OINTMENT OR GEL OR EMULS?

=> s L17 and l15
L18           20 L17 AND L15

=> duplicate
ENTER REMOVE, IDENTIFY, ONLY, OR (?):remove
ENTER L# LIST OR (END):l18
DUPLICATE PREFERENCE IS 'CAPLUS, MEDLINE, USPATFULL, BIOSIS, EMBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L18
L19            19 DUPLICATE REMOVE L18 (1 DUPLICATE REMOVED)

=> d ibib abs kwic 1-5

L19  ANSWER 1 OF 19  USPATFULL
ACCESSION NUMBER:         2000:160984  USPATFULL
```

TITLE: Conformationally constrained LH-RH analogues, their uses and pharmaceutical compositions containing them

INVENTOR(S): Delansorne, Remi, Nice, France
Paris, Jacques, Nice, France
PATENT ASSIGNEE(S): Laboratoire THERAMEX, Monaco (non-U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6153587	20001128
APPLICATION INFO.:	US 1999-317125	19990524 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. WO 1997-EP6322, filed on 12 Nov 1997	
PRIORITY INFORMATION:	EP 1996-402441	19961114

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Russel, Jeffrey E.
LEGAL REPRESENTATIVE: Dennison, Scheiner, Schultz & Wakeman
NUMBER OF CLAIMS: 37
EXEMPLARY CLAIM: 1
LINE COUNT: 1588

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB LH-RH analogues with excellent affinity for LH-RH receptors, of the formula A.sub.1 -A.sub.2 -W-A.sub.3 -A.sub.4 -SPL-A.sub.5 -A.sub.6 -Pro-Z(I) in which:

-A.sub.1 is pGlu, AcSar or an aromatic D-amino acid;

-A.sub.2 is a direct bond, His, DPhe, DpFPhe or DpClPhe;

*W is an aromatic L- or D-amino acid;

-A.sub.3 is Ala, Thr, Ser, DSer, Ser(OBzl) or MeSer;

-A.sub.4 is Tyr, Phe, cPzACAla, L- or D-PicLys, L- or D-NicLys or L- or D-IprLys;

*SPL is the spirolactam of formula: ##STR1## -A.sub.5 is an amino acid with a (C.sub.1 -C.sub.8)alkyl or (C.sub.3-C.sub.6)cycloalkyl side chain;

-A.sub.6 is L- or D-(Arg, HArg, Lys, HLys, Orn, Cit, HCit or Aph), where L- or D-(Arg and HArg) can be substituted by one or two (C.sub.1 -C.sub.4)alkyl groups and L- or D-(Lys, HLys, Orn and Aph) can be substituted by an isopropyl, nicotinoyl or picolinoyl group; and

*Z is GlyNH.sub.2, DAlaNH.sub.2, AzaGlyNH.sub.2 or --NHR.sub.1 where R.sub.1 is a (C.sub.1 -C.sub.4)alkyl optionally substituted by a hydroxy or one or several fluorine atoms, a (C.sub.3 -C.sub.6)cycloalkyl or a heterocyclic radical selected from the group consisting of morpholinyl, pyrrolidinyl and piperidyl;

or its pharmaceutically acceptable salts.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . in combination with antiestrogens such as tamoxifen, raloxifen or droloxifen and the like, or with aromatase inhibitors such as atamestane, **formestane**, letrozole, anastrozole and the like or else with C.sub.17-20 lyase inhibitors such as abiraterone and the like, but also of. . .

SUMM . . . term pituitary-gonadal suppressive indications are slow-release implantable devices, or injectable biodegradable polymeric micro- or nano-particles or -capsules, or micro- or nano-**emulsions**, with unit doses of the peptides or of their appropriate salts ranging from 1 mg to 100 mg per human. . .

SUMM . . . bolus injections, or prolonged continuous, pulsatile or planned perfusions or microinfusions using the appropriate pump technology; gas-propelled subcutaneous microinjection; vaginal **creams**, **gels** or pessaries; rectal enemas or suppositories; transdermal **creams**, **gels**, lotions, solutions, patches or iontophoretic devices; nasal spray or dry powder inhalation device; ophthalmic solutions, **gels**, **creams** or contact lenses; pulmonary inhalation of micro- or nano-particles or droplets

generated manually or with an appropriate pulverization device.

SUMM . . . gastrointestinal degradation and to release them when needed. All other formulations to be taken orally such as solutions, suspensions, syrups, **gels** and the like, or lingual, sublingual or chewable formulations are suited provided that the dosage is increased.

L19 ANSWER 2 OF 19 USPATFULL

ACCESSION NUMBER:	2000:80885 USPATFULL
TITLE:	Taxanes
INVENTOR(S):	Swindell, Charles S., Merion, PA, United States Shashoua, Victor E., Brookline, MA, United States Bradley, Matthews O., Laytonsville, MD, United States Webb, Nigel L., Bryn Mawr, PA, United States
PATENT ASSIGNEE(S):	Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6080877	20000627
APPLICATION INFO.:	US 1997-868476	19970603 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1996-651429, filed on 22 May 1996, now abandoned	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Trinh, Ba K.	
LEGAL REPRESENTATIVE:	Wolf, Greenfield & Sacks, P.C.	
NUMBER OF CLAIMS:	12	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	27 Drawing Figure(s); 14 Drawing Page(s)	
LINE COUNT:	1034	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides taxanes that are conjugates of cis-docosahexaenoic acid and taxotere. The conjugates are useful in treating cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . estrogen agonists; estrogen antagonists; etanidazole; etoposide phosphate; exemestane; fadrozole; fazarabine; fenretinide; filgrastim; finasteride; flavopiridol; fiezelastine; fluasterone; fludarabine; fluorodaunorunicin hydrochloride; forfenimex; **formestane**; fostriecin; fotemustine; gadolinium texaphyrin; gallium nitrate; galocitabine; ganirelix; gelatinase inhibitors; gemcitabine; glutathione inhibitors; hepsulfam; heregulin; hexamethylene bisacetamide; hypericin; ibandronic acid;. . .

DETD . . . active compound. Other compositions include suspensions in aqueous liquors or non-aqueous liquids such as a syrup, an elixir, or an **emulsion**.

L19 ANSWER 3 OF 19 USPATFULL

ACCESSION NUMBER:	2000:12790 USPATFULL
TITLE:	Control of hair growth
INVENTOR(S):	Messenger, Andrew Guy, Sheffield, United Kingdom
PATENT ASSIGNEE(S):	The Central Sheffield University Hospitals NHS Trust, Sheffield, United Kingdom (non-U.S. corporation) Bio-Scientific Ltd, London, United Kingdom (non-U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 6020327	20000201	
	WO 9608231	19980321	
APPLICATION INFO.:	US 1997-809135	19970314	(8)
	WO 1995-GB2166	19950913	
		19970314	PCT 371 date
		19970314	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1994-18484	19940914
	GB 1994-18547	19940915
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Spivack, Phyllis G.	
LEGAL REPRESENTATIVE:	Klauber & Jackson	
NUMBER OF CLAIMS:	10	

EXEMPLARY CLAIM: 1
LINE COUNT: 646
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for treating hair loss is disclosed by topically adminstering an aromatase inhibitor to a mammal, including humans, on the area to be treated.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM Alternatively, the preparation may take the form of a **cream**, shampoo, conditioner or spray.
SUMM . . . anticipated that side effects will be minimised by topical application. This can be achieved by way of a lotion or **cream**, including the usual excipients, creme base, stabilisers etc, or by way of a shampoo, conditioner, or spray. Such formulations are. . .
SUMM . . . be by any suitable route but the transdermal route is preferred. Topical preparations may be in the form of a **cream**, shampoo, conditioner or spray.
SUMM Liquid preparations may be in the form of, for example, aqueous or oily suspensions, solutions, **emulsions**, or may be presented as a dry product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents, **emulsifying** agents, non-aqueous vehicles and, if desired, conventional flavoring, perfuming, or colouring agents.
IT 427-51-0, Cyproterone acetate **566-48-3**, 4-Hydroxyandrostenedione
(hair growth stimulant compns. contg. aromatase inhibitor)

L19 ANSWER 4 OF 19 USPATFULL
ACCESSION NUMBER: 2000:7290 USPATFULL
TITLE: Combined use of GnRH agonist and antagonist
INVENTOR(S): Suzuki, Nobuhiro, Tsukuba, Japan
Furuya, Shuichi, Tsukuba, Japan
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Osaka, Japan (non-U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 6015789	20000118	
	WO 9740846	19971106	
APPLICATION INFO.:	US 1997-894317	19970814	(8)
	WO 1997-JP1459	19970425	
		19970814	PCT 371 date
		19970814	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1996-109790	19960430
	JP 1996-138873	19960531

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Moezie, F. T.
LEGAL REPRESENTATIVE: Wenderoth, Lind & Ponack, L.L.P.
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
LINE COUNT: 7339
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a pharmaceutical luteinizing hormone releasing hormone agonist in combination with a luteinizing hormone releasing hormone antagonist. By using a luteinizing hormone releasing hormone agonist and a luteinizing hormone releasing hormone antagonist in combination, the transient exacerbation with elevation of serum testosterone and estrogen owing to the pituitary-gonadotropic action (acute action) manifested immediately following an initial dose of the luteinizing hormone releasing hormone agonist can be successfully obviated.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . toremifene citrate, etc.), mepitiostane, testrolactone, aminoglutethimide, droloxifene, epitiostanol, ethinylestradiol sulfonate, aromatase inhibitors (e.g. fadrozole hydrochloride, anastrozole, letrozole, Excemestane, danazol (Bonzol), **formestane**, etc.), antiandrogens (e.g. flutamide, bicalutamide, nilutamide, etc.), 5.alpha.-reductase inhibitors (e.g. finasteride, epristeride, etc.), adrenocorticoids (e.g. dexamethasone, prednisolone,

betamethasone, triamcinolone, etc.),. . .

SUMM . . . oral agents (e.g. diluted powders, granules, capsules and tablets), injections, dropping injections, external agents (e.g. transnasal preparations, percutaneous preparations, etc.), **ointments** (e.g. rectal **ointment**, vaginal **ointment**, etc.) and the like.

SUMM . . . chloride, mannitol, sorbitol, glucose, etc.) and the like or in a form of an oily injection by dissolving, suspending or **emulsifying** in plant oil (e.g. olive oil, sesame oil, cotton seed oil, corn oil, etc.), propylene glycol and the like.

SUMM . . . the case of the injection. In the case of a semisolid composition, the preferred one is an aqueous or oily **gel** or an **ointment**. Each of them may be compounded with a pH adjusting agent (e.g. carbonic acid, phosphoric acid, citric acid, hydrochloric acid,. . .

SUMM In the manufacture of an **ointment** for example, the compound of the present invention or a salt thereof can be made into an oily or an aqueous solid, semisolid or liquid **ointment**. Examples of the oily base material applicable in the above-mentioned composition are glycerides of higher fatty acids [e.g. cacao butter,. . . Examples of the aqueous base material are polyethylene glycols and propylene glycol and those of the base material for aqueous **gel** are natural gums, cellulose derivatives, vinyl polymers, acrylic acid polymers, etc.

SUMM . . . per se known technique, the particularly preferred are the sustained-release microcapsules manufactured by the method which comprises preparing a W/O **emulsion** using a liquid containing a water-soluble active substance and a drug carrier [such as a natural or synthetic **gel**-forming substance (e.g. gelatin) or a macromolecular substance (e.g. polyvinyl alcohol)] as an internal phase and a solution of a high. . . thickening the internal phase to a viscosity of at least about 5000 cps or even solidifying it, and subjecting the **emulsion** to a in-water drying process (JP-A 57087/1989) or the sustained-release microcapsules manufactured by the method which comprises preparing a W/O **emulsion** using an internal water phase containing about 20-70 weight % of a bioactive polypeptide and an oil phase containing a. . . ratio of 80/20-100/0 and a weight average molecular weight of 7,000-30,000 as a release control agent and microencapsulating the W/O **emulsion** (JP-A 321622/1992).

DETD . . . by distilling off the solvent under reduced pressure. The residue thus obtained was subjected to a purification procedure of silica **gel** column chromatography to give a yellow amorphous product (1.80 g, 96%).

DETD . . . SO.sub.4), followed by distilling off the solvent under reduced pressure. The residue was subjected to a purification procedure of silica **gel** column chromatography to give a colorless amorphous product (1.00 g, 86%). Thus obtained amorphous product was dissolved in chloroform, and. . .

DETD . . . dichloromethane. Using a benchtop homogenizer (Polytron, Kinematica, Switzerland), the mixture is agitated for about 60 seconds to prepare a W/O **emulsion**. This **emulsion** is poured in 1000 ml of 0.25% aqueous solution of polyvinyl alcohol (PVA) preadjusted to 15.degree. C., and using the benchtop homogenizer, processed into a W/O/W **emulsion**. This W/O/W **emulsion** is further agitated to evaporate dichloromethane and thereby solidify the internal W/O **emulsion**. The product is collected by centrifugation and redispersed in distilled water. This dispersion is further centrifuged to wash out the. . .

DETD . . . dichloromethane. Using a benchtop homogenizer (Polytron, Kinematica, Switzerland), the mixture is agitated for about 60 seconds to prepare a W/O **emulsion**. This **emulsion** is poured in 1000 ml of 0.25% aqueous solution of polyvinyl alcohol (PVA) preadjusted to 15.degree. C. and processed in the benchtop homogenizer to prepare a W/O/W **emulsion**. This W/O/W **emulsion** is further agitated to evaporate dichloromethane and thereby solidify the internal W/O **emulsion**. The product is collected by centrifugation and redispersed in distilled water. This dispersion is further centrifuged to wash out the. . .

L19 ANSWER 5 OF 19 USPATFULL

ACCESSION NUMBER: 2000:4808 USPATFULL

TITLE: Indolocarbazole derivatives useful for the treatment of neurodegenerative diseases and cancer

INVENTOR(S): Roder, Hanno, Ratingen, Germany, Federal Republic of

Lowinger, Timothy B., Nishinomiya, Japan
Brittelli, David R., Branford, CT, United States
VanZandt, Michael C., Guilford, CT, United States

PATENT ASSIGNEE(S): Bayer Corporation, Pittsburgh, PA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6013646	20000111
APPLICATION INFO.:	US 1998-109131	19980702 (9)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Shah, Mukund J.
ASSISTANT EXAMINER: Kifle, Bruck
LEGAL REPRESENTATIVE: Wolf, Greenfield & Sacks, P.C.
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 1457
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel indolocarbazole derivatives potentially useful for the treatment of dementias characterized by tau hyperphosphorylation [Alzheimer's disease (AD), frontal lobe degeneration (FLD), argyrophilic grains disease, subacute sclerotizing panencephalitis (SSPE) as a late complication of viral infections in the CNS], and cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DRWD FIG. 3 is a drawing of a pair of **gels** showing neonatal rat tau phosphorylation in vitro by PK40 without and with prior dephosphorylation by PP2B.

DETD . . . active compound. Other compositions include suspensions in aqueous liquors or non-aqueous liquids such as a syrup, an elixir, or an **emulsion**.

DETD . . . estrogen agonists; estrogen antagonists; etanidazole; etoposide phosphate; exemestane; fadrozole; fazarabine; fenretinide; filgrastim; finasteride; flavopiridol; flezelastine; fluasterone; fludarabine; fluorodaunorunicin hydrochloride; forfenimex; **formestane**; fostriecin; fotemustine; gadolinium texaphyrin; gallium nitrate; galocitabine; ganirelix; gelatinase inhibitors; gemcitabine; glutathione inhibitors; hepsulfam; heregulin; hexamethylene bisacetamide; hypericin; ibandronic acid;. . .

DETD . . . the brown mixture. After stirring the mixture for 2 hours, the solution was filtered through a short pad of silica **gel** and concentrated in vacuo. Purification by flash chromatography (silica, 80-100% CH.sub.2 Cl.sub.2 -hexanes) afforded the target ketone as a yellow. . .

DETD 25 mL of total cell lysate was run on a 10% tris-glycine polyacrylamide **gels** (Novex, 1.5 mm.times.10 well) at 100 volts for 2.5 hors and Western-blotted on nitrocellulose (Novex) overnight at 23 volts or. . .

DETD . . . with PK40. Western-blots were stained with mAb Tau-1 (FIG. 2A, B, upper panels) or AT8 (FIG. 2C, lanes 4-6). Relative **gel** mobilities and loading were visualized by Tau-1 after complete unmasking of the epitope by phosphatase treatment on the blot (FIGS.. . .

DETD . . . in tau properties as isolated from SY5Y cells. Only in this state the electrophoretic mobility of tau matches exactly the **gel** mobility of the corresponding pathologically phosphorylated splice isoform extracted from tangles (FIG. 2C). In cells, the same abnormal phosphorylation state. . .

DETD In order to demonstrate that the small changes in immunochemical and **gel** mobility properties observed in the data presented herein is useful and a relevant model for assessing the large AD-like hyperphosphorylation. . .

DETD . . . (FIG. 4). Compared to control cells (lane C) 1 .mu.M okadaic acid induced ERK2 phosphorylation/activation, as shown by a small **gel** mobility shift of ERK2 (lane OA) and induction of reactivity with a mAb sensitive to the double phosphorylation of the. . . was the prevention of OA induced tau hyperphosphorylation, as tracked by elimination of Tau-1 reactivity and prevention of a small **gel** mobility shift typical of AD-like tau. Note that at 10 .mu.M, with ERK2 activation completely arrested, the tau phosphorylation state. . .

=> d ibib abs kwic 6-20

L19 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:613668 CAPLUS
DOCUMENT NUMBER: 131:223974
TITLE: Medicament for preventing and/or treating a mammary carcinoma containing a steroidal aromatase inhibitor
INVENTOR(S): Schmidt, Alfred; Wieland, Heinrich
PATENT ASSIGNEE(S): S. W. Patentverwertungs G.m.b.H., Austria
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9947143	A1	19990923	WO 1999-EP1374	19990303
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 943333	A1	19990922	EP 1998-104949	19980318
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 9931434	A1	19991011	AU 1999-31434	19990303
BR 9908885	A	20001121	BR 1999-8885	19990303
EP 1063998	A1	20010103	EP 1999-913218	19990303
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: EP 1998-104949 19980318
WO 1999-EP1374 19990303

AB Disclosed is the use of a steroidal aromatase inhibitor e.g. **Formestane**, for producing a medicament formulated for topical use, for preventing and/or treating a mammary carcinoma. The medicament provides a way of avoiding the side effects assocd. with systematic use. It is thus possible to carry out a primary preventative treatment or else a secondary preventative treatment after the appearance of a mammary carcinoma.

REFERENCE COUNT: 8
REFERENCE(S): (2) Brodie, A; Steroids 1981, V38(6), P693 CAPLUS
(3) Clive, C; WO 9325548 A 1993 CAPLUS
(4) Mauvais-Jarvis, P; WO 8503228 A 1985 CAPLUS
(5) S W Patentverwertungs Ges M B H; WO 9736570 A 1997 CAPLUS
(6) Schering AG; EP 0310542 A 1989 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Disclosed is the use of a steroidal aromatase inhibitor e.g. **Formestane**, for producing a medicament formulated for topical use, for preventing and/or treating a mammary carcinoma. The medicament provides a way of avoiding the side effects assocd. with systematic use. It is thus possible to carry out a primary preventative treatment or else a secondary preventative treatment after the appearance of a mammary carcinoma.

ST mammary carcinoma topical steroidal aromatase inhibitor; **Formestane** topical pharmaceutical mammary carcinoma

IT Drug delivery systems
(**emulsions**; topical steroidal aromatase inhibitor for preventing and/or treating mammary carcinoma)

IT Drug delivery systems
(**gels**; topical steroidal aromatase inhibitor for preventing and/or treating mammary carcinoma)

IT Drug delivery systems
(**ointments, creams**; topical steroidal aromatase inhibitor for preventing and/or treating mammary carcinoma)

IT Drug delivery systems
(**ointments**; topical steroidal aromatase inhibitor for preventing and/or treating mammary carcinoma)

IT **566-48-3, Formestane 566-48-3D, Formestane**, derivs. **61630-32-8**

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical steroidal aromatase inhibitor for preventing and/or treating mammary carcinoma)

L19 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:244528 CAPLUS
DOCUMENT NUMBER: 130:291607
TITLE: Tightening and/or reducing the size of body parts containing fat cells
INVENTOR(S): Schmidt, Alfred; Wieland, Heinrich
PATENT ASSIGNEE(S): S.W. Patentverwertungs G.m.b.H., Austria
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9917712	A2	19990415	WO 1998-EP6085	19980924
WO 9917712	A3	19990722		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9896278	A1	19990427	AU 1998-96278	19980924
EP 1021191	A2	20000726	EP 1998-950078	19980924
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9812859	A	20000808	BR 1998-12859	19980924
PRIORITY APPLN. INFO.:			DE 1997-19744451	19971008
			WO 1998-EP6085	19980924

AB Estrogen antagonists or aromatase inhibitors are applied locally to tighten and/or reduce the size of body parts contg. fat cells, e.g. for female breast redn. The substances are highly effective and well tolerated, and eliminate the need for surgical redn. by locally inhibiting extragonadal estrogen formation; the decrease in local estrogen concn. results in a decrease in conversion of connective tissue cells to fat cells, a decrease in lipid accumulation in the fat cells, and a tightening and smoothing of the skin in the treated area. Thus, application to the breasts of a **cream** contg. urea 10.0, TiO2 15.0, Vaseline 25.0, iso-Pr palmitate 10.0, hydrogenated peanut oil 10.0, Tween 80 5.0, 4-hydroxyandrostenedione (aromatase inhibitor) 1.5, and H2O to 100.0 g resulted in a decrease in vol. of 10% after 12 wk and 30% after 24 wk.
AB Estrogen antagonists or aromatase inhibitors are applied locally to tighten and/or reduce the size of body parts contg. fat cells, e.g. for female breast redn. The substances are highly effective and well tolerated, and eliminate the need for surgical redn. by locally inhibiting extragonadal estrogen formation; the decrease in local estrogen concn. results in a decrease in conversion of connective tissue cells to fat cells, a decrease in lipid accumulation in the fat cells, and a tightening and smoothing of the skin in the treated area. Thus, application to the breasts of a **cream** contg. urea 10.0, TiO2 15.0, Vaseline 25.0, iso-Pr palmitate 10.0, hydrogenated peanut oil 10.0, Tween 80 5.0, 4-hydroxyandrostenedione (aromatase inhibitor) 1.5, and H2O to 100.0 g resulted in a decrease in vol. of 10% after 12 wk and 30% after 24 wk.

IT Wrinkle-preventing cosmetics
(**creams**; tightening or reducing size of body parts contg. fat cells)

IT Skin **creams**
(wrinkle-preventing; tightening or reducing size of body parts contg. fat cells)

IT **566-48-3**, 4-Hydroxyandrostenedione
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aromatase inhibitor; tightening or reducing size of body parts contg. fat cells)

L19 ANSWER 8 OF 19 USPATFULL
ACCESSION NUMBER: 1999:75671 USPATFULL
TITLE: Taxane compounds and compositions
INVENTOR(S): Bradley, Matthews O., Laytonville, MD, United States
Shashoua, Victor E., Brookline, MA, United States
Swindell, Charles S., Merion, PA, United States
Webb, Nigel L., Bryn Mawr, PA, United States
PATENT ASSIGNEE(S): Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5919815	19990706
APPLICATION INFO.:	US 1996-653951	19960522 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Reamer, James H.
LEGAL REPRESENTATIVE: Wolf, Greenfield & Sacks, P.C.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1,4
NUMBER OF DRAWINGS: 27 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 940
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides taxanes that are conjugates of cis-docosahexaenoic acid and paclitaxel. The conjugates are useful in treating cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . estrogen agonists; estrogen antagonists; etanidazole; etoposide phosphate; exemestane; fadrozole; fazarabine; fenretinide; filgrastim; finasteride; flavopiridol; flezelastine; fluasterone; fludarabine; fluorodaunorunicin hydrochloride; forfenimex; **formestane**; fostriecin; fotemustine; gadolinium texaphyrin; gallium nitrate; galocitabine; ganirelix; gelatinase inhibitors; gemcitabine; glutathione inhibitors; hepsulfam; heregulin; hexamethylene bisacetamide; hypericin; ibandronic acid;. . .
DETD . . . active compound. Other compositions include suspensions in aqueous liquors or non-aqueous liquids such as a syrup, an elixir, or an **emulsion**.

L19 ANSWER 9 OF 19 USPATFULL
ACCESSION NUMBER: 1999:61173 USPATFULL
TITLE: Treatment of male climacteric disorders with nitric oxide synthase substrates and/or donors, in combination with androgens and/or aromatase inhibitors
INVENTOR(S): Chwalisz, Kristof, Berlin, Germany, Federal Republic of
Garfield, Robert E., Friendswood, TX, United States
PATENT ASSIGNEE(S): Schering Aktiengesellschaft and Board of Regents, Berlin, Germany, Federal Republic of (non-U.S. corporation)
The University of Texas System, Austin, TX, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5906987	19990525
APPLICATION INFO.:	US 1997-812912	19970310 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Jordan, Kimberly
LEGAL REPRESENTATIVE: Millen, White, Zelano & Branigan, P.C.
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 689
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The symptoms of climacterium in male mammals, e.g., hypertension, cardiovascular disease and osteoporosis, are ameliorated by the administration to an afflicted individual one or both of a nitric oxide substrate and/or nitric acid donor, in combination with an androgen, an aromatase inhibitor or both, wherein the circulating levels of testosterone in the afflicted individual are increased.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . selective aromatase inhibitors according to this invention are, for example, the steroidal compounds 1-Methyl-androsta-1,4-diene-3,17-

dione (DE-A 33 22 285; atamestane); 4-hydroxy-4-androstene-3,17-dione (**formestane**); as well as the non-steroidal aromatase inhibitors: (RS)-5-(4-cyanophenyl)-5,6,7,8-tetrahydro-imidazo-(1,5.alpha.)-pyridine, hydrochloride (Cancer Res., 48, pp. 834-838, 1988: fadrozole); 4-[cyano-.alpha.-(1,2,4-triazol-1-yl)-benzyl]-benzonitrile (CGS 20267), 5-[cyclopentylidene-(1-imidazolyl)-methyl]-thiophene-2-carbonitrile(EP-A. . .

DETD The pharmaceutical preparations can be sterilized and if desired mixed with auxiliary agents, e.g., lubricants, preservatives, stabilizers, wetting agents, **emulsifiers**, salts for influencing osmotic pressure, buffers, coloring, flavoring and/or aromatic substances and the like which do not deleteriously react with. . .

DETD For parental application, particularly suitable are solutions, preferably oily or aqueous solutions, as well as suspensions, **emulsions**, or implants, including suppositories, transdermal patches, and vaginal **gels**, **creams** and foams. Ampoules are convenient unit dosages. In a preferred aspect, the composition of this invention is adapted for ingestion.

L19 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:87617 CAPLUS
DOCUMENT NUMBER: 128:149982
TITLE: Use of sex steroid function modulators to treat wounds and fibrotic disorders
INVENTOR(S): Ferguson, Mark William James; Ashcroft, Gillian Sarah
PATENT ASSIGNEE(S): Victoria University of Manchester, UK; Ferguson, Mark William James; Ashcroft, Gillian Sarah
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9803180	A2	19980129	WO 1997-GB1973	19970722
WO 9803180	A3	19980604		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2261263	AA	19980129	CA 1997-2261263	19970722
AU 9736288	A1	19980210	AU 1997-36288	19970722
ZA 9706480	A	19990122	ZA 1997-6480	19970722
EP 930876	A2	19990728	EP 1997-932922	19970722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000515523	T2	20001121	JP 1998-506706	19970722
PRIORITY APPLN. INFO.:			GB 1996-15348	19960722
			GB 1997-1600	19970127
			WO 1997-GB1973	19970722

AB The present application relates to the use of compds. that influence the sex hormone system for the treatment of wounds and/or fibrotic disorders. Preferred compds. for use in such treatments are steroid hormones and esp. the estrogens. Compns. contg. the compds. of the invention are also claimed.

IT Drug delivery systems
(**creams**; use of sex steroid function modulators to treat wounds and fibrotic disorders)

IT Drug delivery systems
(**ointment**; use of sex steroid function modulators to treat wounds and fibrotic disorders)

IT Drug delivery systems
Eye drops
Fibrosis
Gels (drug delivery systems)
Hydrogels (drug delivery systems)
Implants (drug delivery systems)
Liquid dosage forms (drug delivery systems)

Wound healing promoters
(use of sex steroid function modulators to treat wounds and fibrotic disorders)

IT 50-27-1, Estriol 50-28-2, Estradiol, biological studies 50-41-9, Clomiphene citrate 53-43-0, DHEA 56-53-1, Stilbestrol 57-63-6, Ethinylestradiol 57-83-0, Progesterone, biological studies 72-33-3, Mestranol 84-17-3, Dienestrol 427-51-0, Cyproterone acetate 434-22-0, Nandrolone 481-97-0, Estrone 3-sulfate **566-48-3**, **Formestane** 651-48-9, DHEA sulfate 2624-43-3, Cyclofenil 4719-75-9 5630-53-5, Tibolone 7280-37-7, Piperazine estrone sulfate 10418-03-8, Stanozolol 10540-29-1, Tamoxifen 13311-84-7, Flutamide 28014-46-2, Polyestradiol phosphate 102676-31-3, Fadrozole hydrochloride 107868-30-4, Exemestane 120511-73-1, Anastrozole
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of sex steroid function modulators to treat wounds and fibrotic disorders)

L19 ANSWER 11 OF 19 USPATFULL
ACCESSION NUMBER: 1998:98932 USPATFULL
TITLE: DHA-pharmaceutical agent conjugates of taxanes
INVENTOR(S): Shashoua, Victor E., Brookline, MA, United States
Swindell, Charles S., Merion, PA, United States
Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
PATENT ASSIGNEE(S): Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5795909	19980818
APPLICATION INFO.:	US 1996-651312	19960522 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Jarvis, William R. A.
LEGAL REPRESENTATIVE: Wolf, Greenfield & Sacks, P.C.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 27 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 2451
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of cis-docosahexaenoic acid and taxanes useful in treating cell proliferative disorders. Conjugates of paclitaxel and docetaxel are preferred.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . estrogen agonists; estrogen antagonists; etanidazole; etoposide phosphate; exemestane; fadrozole; fazarabine; fenretinide; filgrastim; fmasteride; flavopiridol; flezelastine; fluasterone; fludarabine; fluorodaunorunicin hydrochloride; forfenimex; **formestane**; fostriecin; fotemustine; gadolinium texaphyrin; gallium nitrate; galocitabine; ganirelix; gelatinase inhibitors; gemcitabine; glutathione inhibitors; hepsulfam; heregulin; hexamethylene bisacetamide; hypericin; ibandronic acid;. . .
DETD . . . flunarizine; fluocalcitriol; fluorodaunorunicin hydrochloride; fluoxetine, R-; fluoxetine, S-; fluparoxan; flupirtine; flurbiprofen axetil; flurithromycin; fluticasone propionate; flutrimazole; fluvastatin; fluvoxamine; forasartan; forfenimex; **formestane**; formoterol; formoterol, R,R-; fosfomycin; trometamol; fosinopril; fosphenytoin; fostriecin; fotemustine; gabapentin; gadobenic acid; gadobutrol; gadodiamide; gadodiamide-EOB-DTPA; gadolinium texaphyrin; gadoteric acid; gadoteridol;. . .
DETD . . . active compound. Other compositions include suspensions in aqueous liquors or non-aqueous liquids such as a syrup, an elixir, or an **emulsion**.

L19 ANSWER 12 OF 19 USPATFULL
ACCESSION NUMBER: 1998:45195 USPATFULL
TITLE: Combination for treatment of proliferative diseases
INVENTOR(S): Muller, Marcel, Allschwil, Switzerland
Geiger, Thomas, Freiburg, Germany, Federal Republic of
Altmann, Karl-Heinz, Reinach, Switzerland
Fabbro, Doriano, Arlesheim, Switzerland
Dean, Nicholas M., Encinitas, CA, United States
Monia, Brett, Carlsbad, CA, United States

Bennett, Clarence Frank, Carlsbad, CA, United States
PATENT ASSIGNEE(S): Novartis Corporation, Summit, NJ, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5744460	19980428
APPLICATION INFO.:	US 1996-612775	19960307 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Robinson, Douglas W.
ASSISTANT EXAMINER: Nelson, Amy J.
LEGAL REPRESENTATIVE: Nowak, Henry P.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 2910
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to combinations of PKC-targeted (especially PKC-.alpha.-targeted) deoxyribo- and ribo-oligonucleotides and derivatives thereof with other chemotherapeutic compounds, as well as to pharmaceutical preparations and/or therapies, in relation to disease states which respond to such oligonucleotides or oligonucleotide derivatives, especially to to modulation of the activity of a regulatory protein. In particular, the invention relates to products or combinations comprising antisense oligonucleotides or oligonucleotide derivatives targeted to nucleic acids encoding human PKC and other (preferably standard) chemotherapeutics, either in fixed combination or for chronologically staggered or simultaneous administration, and the combined use of both classes of compounds, either in fixed combination or for chronologically staggered or simultaneous administration, for the treatment of proliferative diseases, especially tumor diseases, that can be treated by inhibition of PKC activity, that is, where the antisense oligonucleotides or oligonucleotide derivatives are targeted to nucleic acids encoding the regulatory protein PKC or active mutated derivatives thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . and can thus greatly enhance the efficiency of antisense inhibition. Cleavage of the RNA target can be routinely demonstrated by **gel** electrophoresis. In another embodiment, the chimeric oligonucleotide is also modified to enhance nuclease resistance. Cells contain a variety of exo-. . . thereof with cellular extracts or isolated nuclease solutions and measuring the extent of intact oligonucleotide remaining over time, usually by **gel** electrophoresis. Oligonucleotides which have been modified to enhance their nuclease resistance survive intact for a longer time than unmodified oligonucleotides.. . .

SUMM . . . leuprolide (Lupron, Lupron Depot); anti-androgens such as flutamide (Eulexin); anti-estrogens such as tamoxifen; aromatase inhibitors such as aminogluthetimide (Cytadren), lentaron (**Formestane**, 4-hydroxy-4-androsten-3,17-dione) (see EP 0 162 510), fadrozole (5-(p-cyanophenyl)-5,6,7,8-tetrahydroimidazo [1,5-a]pyridin, see EP 0 437 415 and EP 0 165 904), letrozole. . .

SUMM . . . leuprolide (Lupron, Lupron Depot); anti-androgens such as flutamide (Eulexin); anti-estrogens such as tamoxifen; aromatase inhibitors such as aminogluthetimide (Cytadren), lentaron (**Formestane**, 4-hydroxy-4-androsten-3,17-dione) (see EP 0 162 510), fadrozole (5-(p-cyanophenyl)-5,6,7,8-tetrahydroimidazo [1,5-a]pyridin, see EP 0 437 415 and EP 0 165 904), letrozole. . .

IT 50-02-2, Dexamethasone 50-28-2, Estradiol, biological studies 50-44-2, 6-Mercaptopurine 50-76-0, Dactinomycin 50-91-9, 5-Fluorodeoxyuridine 51-21-8, 5-Fu 52-24-4, Triethylenethiophosphoramide 53-03-2, Prednisone 53-19-0, Mitotane 55-98-1, Busulfan 56-53-1, Diethylstilbestrol 57-22-7, Vincristine 58-22-0, Testosterone 59-05-2, Methotrexate 60-34-4D, Methylhydrazine, derivs. 68-96-2, Hydroxyprogesterone 76-43-7, Fluoxymesterone 84-65-1, Anthraquinone 125-84-8, Aminoglutethimide 147-94-4, Cytosine arabinoside 154-42-7, 6-Thioguanine 290-87-9D, S-Triazine, derivs. 302-79-4, Tretinoin 320-67-2, 5-Azacytidine 520-85-4, Medroxyprogesterone **566-48-3**, Lentaron 595-33-5, Megestrol acetate 865-21-4, Vinblastine 4291-63-8, Cladribine 4342-03-4, Dacarbazine 4891-15-0, Estracyt 9015-68-3, Asparaginase 10540-29-1, Tamoxifen 13311-84-7, Flutamide 18378-89-7, Plicamycin 18883-66-4, Streptozocin 20830-81-3, Daunorubicin 29767-20-2, Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide 51264-14-3,

Amsacrine 52128-35-5, Trimetrexate 53643-48-4, Vindesine 53714-56-0, Leuprolide 53910-25-1, Pentostatin 56420-45-2, Epirubicin 58957-92-9, Idarubicin 63521-85-7, Esorubicin 65807-02-5, Goserelin 75607-67-9, Fludarabine phosphate 83150-76-9, Octreotide 102676-47-1 110942-02-4, Aldesleukin 112809-51-5 120685-11-2, N-Benzoylstaurosporine 143030-47-1 149281-19-6 149400-88-4 157168-02-0 173458-56-5 196102-76-8 196102-77-9 196102-78-0
(combinations of drugs with antisense oligonucleotides for treatment of proliferative diseases)

L19 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:557633 CAPLUS
DOCUMENT NUMBER: 127:239118
TITLE: Drug delivery systems containing ester sunscreens and penetration enhancers
INVENTOR(S): Reed, Barry Leonard; Morgan, Timothy Matthias; Finnin, Barrie Charles
PATENT ASSIGNEE(S): Monash University, Australia; Reed, Barry Leonard; Morgan, Timothy Matthias; Finnin, Barrie Charles
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729735	A1	19970821	WO 1997-AU91	19970219
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9717134	A1	19970902	AU 1997-17134	19970219
AU 706967	B2	19990701		
EP 901368	A1	19990317	EP 1997-904304	19970219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000504697	T2	20000418	JP 1997-528834	19970219
AU 9952589	A1	19991202	AU 1999-52589	19991001
PRIORITY APPLN. INFO.:			AU 1996-8144	19960219
			AU 1997-17134	19970219
			WO 1997-AU91	19970219

OTHER SOURCE(S): MARPAT 127:239118

AB A transdermal drug delivery system which comprises at least one physiol. active agent or prodrug thereof and at least one dermal penetration enhancer; characterized in that the dermal penetration enhancer is a safe skin-tolerant ester sunscreen. A non-occlusive, percutaneous or transdermal drug delivery system which comprises: (1) an effective amt. of at least one physiol. active agent or prodrug thereof; (2) at least one non-volatile dermal penetration enhancer; and (3) at least one volatile liq.; characterized in that the dermal penetration enhancer is adapted to transport the physiol. active agent across a dermal surface or mucosal membrane of an animal, including a human, when the volatile liq. evaps., to form a reservoir or depot of a mixt. comprising the penetration enhancer and the physiol. active agent or prodrug within said surface or membrane; and the dermal penetration enhancer is of low toxicity to, and is tolerated by, the dermal surface or mucosal membrane of the animal. The mean flux of 2% ketoprofen in 70% vol./vol. aq. ethanol through shed snakes kinetics in presence of 2% octyl salicylate in 70% vol./vol. aq. ethanol was 27.66 as compared to 2.58 .mu.g/cm2.h for azone. A transdermal aerosol contained 17.beta.-estradiol 2, octyl dimethyl-p-aminobenzoate 8, ethanol 69, and di-Me ether 30%.

IT **Emulsifying** agents
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery systems contg. ester sunscreens and penetration enhancers)

IT 51-34-3, Scopolamine 51-98-9, Norethisterone acetate 52-86-8, Haloperidol 57-63-6, Ethinylestradiol 57-83-0, Progesterone, biological studies 58-22-0, Testosterone 58-38-8, Prochlorperazine

69-23-8, Fluphenazine 73-31-4, Melatonin 83-74-9, Ibogaine 90-34-6, Primaquine 92-13-7, Pilocarpine 321-64-2, Tacrine 364-62-5, Metochlopramide 427-51-0, Cyproterone acetate 437-38-7, Fentanyl **566-48-3**, 4-Hydroxy-androstenedione 661-19-8, n-Docosanol 745-65-3, Alprostadil 2363-58-8, Epitiostanol 5104-49-4, Flurbiprofen 10540-29-1, Tamoxifen 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 18559-94-9, Salbutamol 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22232-71-9, Mazindol 23031-25-6, Terbutaline 28981-97-7, Alprazolam 33564-30-6, MK 306 34911-55-2, Bupropion 35121-78-9, Prostacyclin 38304-91-5, Minoxidil 39562-70-4, Nitrendipine 52485-79-7, Buprenorphine 53783-83-8, Tromantadine 61413-54-5, Rolipram 88150-42-9, Amlodipine 89365-50-4, Salmeterol 98319-26-7, Finasteride 99614-02-5, Ondansetron 99755-59-6, n0923 103628-46-2, Sumatriptan 107868-30-4, Exemestane 137099-09-3, Turosteride 146117-78-4, Ly191704
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery systems contg. ester sunscreens and penetration enhancers)

L19 ANSWER 14 OF 19 USPATFULL

ACCESSION NUMBER:	97:17918 USPATFULL
TITLE:	Compositions and methods for enhanced drug delivery
INVENTOR(S):	Hale, Ron L., Woodside, CA, United States Lu, Amy, Los Altos, CA, United States Solas, Dennis, San Francisco, CA, United States Selick, Harold E., Belmont, CA, United States Oldenburg, Kevin R., Fremont, CA, United States Zaffaroni, Alejandro C., Atherton, CA, United States
PATENT ASSIGNEE(S):	Affymax Technologies N.V., Middlesex, England (non-U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5607691	19970304
APPLICATION INFO.:	US 1995-449188	19950524 (8)

RELATED APPLN. INFO.:	Continuation of Ser. No. US 1993-164293, filed on 9 Dec 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-77296, filed on 14 Jun 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-898219, filed on 12 Jun 1992, now abandoned And a continuation-in-part of Ser. No. US 1993-9463, filed on 27 Jan 1993, now abandoned
DOCUMENT TYPE:	Utility
PRIMARY EXAMINER:	Levy, Neil S.
LEGAL REPRESENTATIVE:	Stevens, Lauren L.
NUMBER OF CLAIMS:	5
EXEMPLARY CLAIM:	1
LINE COUNT:	5349

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods of delivering pharmaceutical agents across membranes, including the skin layer or mucosal membranes of a patient. A pharmaceutical agent is covalently bonded to a chemical modifier, via a physiologically cleavable bond, such that the membrane transport and delivery of the agent is enhanced.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . of the charged complex in comparison with the pharmaceutical agent may also be assessed using the above analytical techniques and **gel** or capillary electrophoresis. In general, if a complex shows faster mobility during electrophoresis than the unmodified pharmaceutical agent, then the. . .

DETD . . . such flux can be controlled by either providing a rate-controlling membrane or dispersing the compound in a polymer matrix or **gel**.

DETD . . . The reservoir typically will comprise a pool of electrolyte solution, for example an aqueous electrolyte solution or a hydrophilic, electrolyte-containing, **gel** or **gel** matrix, semi-solid, foam, or absorbent material. Such pharmaceutical agent-chemical modifier complex reservoirs, when electrically connected to the anode or the. . .

DETD . . . prepared by combining the pharmaceutical agent-chemical modifier complex with conventional pharmaceutical diluents and carriers commonly used in topical dry, liquid, **cream** and aerosol formulations. **Ointment** and **creams** may, for example, be formulated with an aqueous or oily base with the addition of suitable

thickening and/or gelling agents.. . .

DETD . . . with an aqueous or oily base and will, in general, also include one or more of the following: stabilizing agents, **emulsifying** agents, dispersing agents, suspending agents, thickening agents, coloring agents, perfumes, and the like.

DETD Dosage forms for the topical administration of a complex of this invention include powders, sprays, **ointments**, pastes, **creams**, lotions, **gels**, solutions, patches and inhalants. The active compound may be mixed under sterile conditions with a pharmaceutically- acceptable carrier, and with. . .

DETD The **ointments**, pastes, **creams** and **gels** also may contain excipients, such as animal and vegetable fats, oils, waxes, paraffins, starch, tragacanth, cellulose derivatives, polyethylene glycols, silicones,. . .

DETD . . . systemic circulation and reduce immediate metabolism by the liver and intestinal wall flora. Transmucosal drug dosage forms (e.g., tablet, suppository, **ointment**, **gel**, pessary, membrane, and powder) are typically held in contact with the mucosal membrane and disintegrate and/or dissolve rapidly to allow. . .

DETD . . . (2.times.30 ml). The remaining solid (102 mg, 0.19 mmol, 24% yield) gave a single major spot on thin-layer chromatography (silica **gel**, methanol/chloroform/water 3/7/0.5) and molecular mass of 504.4 (M.sup.+ -Cl.sup.-) by FAB mass spectrometry.

DETD . . . ml) and choline chloride chloroformate (216 mg, 1.07 mmol) was added. Additional pyridine (3 ml) was added to form a **gel**-like suspension which was stirred overnight at about 35.degree. C. Thin layer chromatography (TLC) (silica **gel**, developed first with chloroform/methanol, 9/1, and then chloroform/methanol/water, 7/3/0.5) indicated only a small amount of product had formed so an. . .

DETD . . . choline chloride chloroformate (175 mg, 0.8 mmol) was added. The heterogeneous mixture was warmed to room temperature and sonicated to **emulsify** and stirring continued overnight. The mixture was evaporated to dryness and the residue triturated with ether and acetone. The solid. . .

DETD . . . ml). Evaporation of the filtrate and the wash gave a total of 370 mg of gummy residue which TLC (silica **gel**, ethanol/chloroform/water 10/5/5) indicated to be a mixture of starting estradiol (R.sub.i 0.9) and product (R.sub.i 0.7). The solid was likewise. . .

DETD . . . product (416 mg) which was shown to be mainly desired compound with a trace of unreacted digitoxigenin by TLC (silica **gel**, first elution with chloroform/methanol 10/1, second elution with chloroform/methanol/water 7/3/0.5).

DETD . . . mixture was concentrated in vacuo and the residue was triturated with ether. The residue was passed through two silanized silica **gel** columns (eluting with 3% methanol in dichloromethane) and was then dissolved in dichloromethane (10 ml) and filtered. Column chromatography (eluting. . .

DETD . . . organic layer was then dried over sodium sulfate, filtered and evaporated to give, after further purification by column chromatography (silica **gel**, 10% ethyl acetate in dichloromethane), 240 mg (57% yield) of the desired product).

DETD . . . with saturated sodium bicarbonate, dried over sodium sulfate and the solvent removed by evaporation. The residue was purified by silica **gel** column chromatography (elution with 1% ethyl acetate in dichloromethane) to give 310 mg (44%) of the enol acetate.

DETD . . . over sodium sulfate and filtered. The filtrate was evaporated to give 117 mg crude product which was purified by silica **gel** column chromatography (elution with 20% ethyl acetate in dichloromethane) to give 92 mg of the hydroxyl diester.

DETD . . . filtered and evaporated to give the 17.beta.-benzyloxycarbonyl derivative (480 mg crude). The material was purified by column chromatography on silica **gel** (5% methanol in dichloromethane) to give the desired compound (325 mg, 81% yield).

DETD . . . layer dried over sodium sulfate, filtered and evaporated to give 310 mg of crude product. Purification by column chromatography (silica **gel**, 10% methanol in dichloromethane) gave the desired ester (200 mg).

DETD . . . filtered and evaporated to give 140 mg of crude deprotected alcohol which was further purified by flash chromatography on silica **gel** using 15% methanol in dichloromethane to give 107 mg (66% yield) of the 17-(norcholine glycinate carbamate) of estradiol.

DETD . . . over sodium sulfate, filtered and solvent evaporated to give 2.1 g of crude product. This material was purified by silica **gel**

column chromatography (elution with dichloromethane) to give 1.57 g (75% yield) of the carbonate ester.

DETD . . . was filtered to remove the precipitated dicyclohexyl urea and the filtrate evaporated to dryness. The residue was purified by silica **gel** flash chromatography in 2/1 dichloromethane/ethyl acetate to give 920 mg (83% yield) of the t-BOC protected aminohexanoic ester.

DETD . . . mixture was filtered to remove the precipitated dicyclohexyl urea and solvents removed by evaporation. The residue was purified by silica **gel** column chromatography using ethyl acetate/dichloromethane mixtures to give 1.14 g (75% yield) of the N-t-BOC-protected aminohexanoic ester.

DETD . . . sulfate, filtered and evaporated to give 1.2 g of crude oily residue. This material was purified by flash chromatography (silica **gel**, 10% ethyl acetate/dichloromethane) to give 0.98 g (97% yield) of the t-BOC-protected amino ester.

DETD . . . over sodium sulfate, filtered and evaporated to give 1.8 g of crude product which was purified by column chromatography (silica **gel**, 3% methanol/dichloromethane) to give 1.2 g (69% yield) of the t-BOC-amino carbonate.

DETD . . . oil which solidified on trituration with ether (3.times.30 ml). The solid (244 mg) was purified by flash chromatography on silica **gel** with elution by 10% methanol in chloroform (200 ml) to remove unreacted digitoxin. Further elution using 20% methanol in chloroform. . .

DETD . . . saturated sodium bicarbonate, dried over sodium sulfate and filtered. The solvent was removed and the residue was purified by silica **gel** column chromatography (elution with 30% ethyl acetate in dichloromethane) to give 1.57 g (45% yield) of the desired bis-ketal.

DETD . . . yield a light yellow solid (130 mg) which was dissolved in 5% methanol in dichloromethane and chromatographed (dry column, silica **gel**) to yield the desired diester (69 mg, 20% yield) whose structure was confirmed by NMR.

DETD . . . dried over sodium sulfate, and concentrated in vacuo to yield crude chloromethyl ester (4.2 g) which was filtered through silica **gel** (eluting with 5% methanol in dichloromethane, 45 ml) to yield pure ester (3.27 g, 89.5% yield) whose structure was confirmed. .

DETD . . . distribution of a sample of a mixture of labeled fragments can be assessed by electrophoresis using a standard DNA sequencing **gel** and autoradiography. See, e.g., Sambrook et al. Molecular Cloning. Typically, a distribution of uniformly labeled fragments extending from approximately 5-200. . .

DETD . . . sec

methyl), iodide salt
theophylline-7-[4-(N,N,N-trimethylamino)-
2.4 hr
butyroyloxymethyl], bromide salt
nalidixic acid, choline ester, bromide salt
66 min
nalidixic acid 6-(N,N,N-trimethylamino)-
4.8 min
hexanoyloxymethyl ester, iodide salt
formestane-4-choline carbonate, bromide salt
26 min
melatonin-1-choline carbamate, bromide salt
15 hr
digoxin-4'"-[(O-acetyl)-betonicine ester],
1.8 min
chloride salt
betonicine-O-acetate 4-nitrophenethyl ester
6 min
digoxin-3',3",12-tris-(6-trimethylaminohexanoyl-
14 hr
oxymethyl. . .

L19 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:363503 CAPLUS
DOCUMENT NUMBER: 125:18659
TITLE: Hair growth stimulant compositions containing an aromatase inhibitor
INVENTOR(S): Messenger, Andrew Guy
PATENT ASSIGNEE(S): University of Sheffield, UK
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9608231	A1	19960321	WO 1995-GB2166	19950913
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2200085	AA	19960321	CA 1995-2200085	19950913
AU 9535253	A1	19960329	AU 1995-35253	19950913
AU 705118	B2	19990513		
GB 2295088	A1	19960522	GB 1995-18725	19950913
GB 2295088	B2	19981125		
EP 777458	A1	19970611	EP 1995-932057	19950913
EP 777458	B1	20001206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10508828	T2	19980902	JP 1995-509999	19950913
AT 197889	E	20001215	AT 1995-932057	19950913
US 6020327	A	20000201	US 1997-809135	19970314

PRIORITY APPLN. INFO.: GB 1994-18484 19940914
GB 1994-18547 19940915
WO 1995-GB2166 19950913
GB 1995-9418547 19950915

AB A method for treating and preventing hair loss by topically administering an aromatase inhibitor to a mammal, including humans, on the area to be treated. Mean aromatase activity was greater in balding (110.0 fmol/g/tissue h) than in non-balding scalp (55.0 fmol/g tissue/h) and addn. of 25 nmol 4-hydroxyandrostenedione (I) reduced activity to background levels. A topical formulation contained propylene glycol 5, ethanol 10, water 85, and I 0.2-10%.

IT Cosmetics
(**creams**, hair growth stimulant compns. contg. aromatase inhibitor)

IT 427-51-0, Cyproterone acetate **566-48-3**, 4-Hydroxyandrostenedione
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(hair growth stimulant compns. contg. aromatase inhibitor)

L19 ANSWER 16 OF 19 USPATFULL
ACCESSION NUMBER: 96:77760 USPATFULL
TITLE: Combination therapy for the treatment of estrogen-sensitive disease
INVENTOR(S): Labrie, Fernand, Quebec, Canada
PATENT ASSIGNEE(S): Endorecherche Inc., Quebec, Canada (non-U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5550107	19960827
APPLICATION INFO.:	US 1991-785890	19911104 (7)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1989-321926, filed on 10 Mar 1989, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Jordan, Kimberly
LEGAL REPRESENTATIVE: Ostrolenk, Faber, Gerb & Soffen, LLP
NUMBER OF CLAIMS: 46
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 1665
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of treatment of breast and endometrial cancer in susceptible warm-blooded animals may include inhibition of ovarian hormonal secretion by surgical (ovariectomy) or chemical (use of an LHRH agonist, e.g. [D-Trp.sup.6, des-Gly-NH.sub.2.sup.10]LHRH ethylamide or antagonist) as part of a combination therapy comprising administering an antiestrogen together with at least one compound selected from the group consisting of an androgen, a progestin, at least one inhibitor of sex

steroid formation, especially 17.beta.-hydroxysteroid dehydrogenase and aromatase activity, at least one inhibitor of prolactin secretion, one inhibitor of growth hormone secretion and one inhibitor of ACTH secretion. Pharmaceutical compositions useful for such treatment and pharmaceutical kits containing such composition are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . cleaved from the resin and deprotected by use of HF. The crude peptide is purified by the usual techniques, e.g., **gel** filtration, HPLC and partition chromatography and optionally lyophilization. See also D. H. Coy et al., J. Med. Chem. 19, pages. . .

DETD . . . dried with anhydrous MgSO.sub.4 and the solvent was removed under reduced pressure. The residue was purified by chromatography on silica **gel**. Elution with mixture of EtOAc/hexane (1.5:8.5 v/v) yielded N-butyl, N-methyl-11-(3'-benzoyloxy-17'-oxo-estra-1',3',5'(10')-trien-7'.alpha.-yl) undecanamide (4.25 g, 96%) as colorless oil; TR .nu. (neat). . . dried with anhydrous MgSO.sub.4 and the solvent was removed under reduced pressure. The residue was purified by chromatography on silica **gel**. Elution with mixture of EtOAc/hexane (3:7 v/v) yielded N-butyl, N-methyl-11-(3'-hydroxy-17'-oxo-estra-1',3',4'(10)-trien-7'.alpha.-yl) undecanamide (2) (294 mg, 97%) as colorless oil; .sup.1 H-NMR. . . v/v) as eluent. The solvent was removed under reduced pressure and, the residue was purified by flash chromatography on silica **gel**. Elution with mixture of EtOAc/hexane (1:4 v/v) yielded the N-butyl, N-methyl-11-(3',17'-diacetoxy-estra-1',3',5'(10'), 16'-tetraen-7'.alpha.-yl) undecamide (3) (244 mg, 80%) as colorless oil;. . .

DETD . . . was washed with water, dried with anhydrous MgSO.sub.4 and evaporated to dryness. The residue was purified by chromatography on silica **gel** carried out with mixture of EtOAc/hexane, (3:7 v/v) to give the N-butyl, N-methyl-11-(16'.alpha.-chloro-3'acetoxy-17'-oxo-estra-1',3',4'(10')-trien-7'.alpha.-yl) undecanamide (4) (115 mg, 89%) as colorless. . .

DETD . . . Na.sub.2 SO.sub.4 and evaporated under reduced pressure. The residue included two important antiestrogens which were separated by chromatography on silica **gel** and eluted with a mixture of EtOAc/hexane (4:6 v/v):

IT 71-58-9, Medroxyprogesterone acetate 76-43-7 125-84-8, Aminoglutethimide **566-48-3**, 4-Hydroxyandrostenedione 25614-03-3, Bromocryptine 34184-77-5, Promegestone 65277-42-1, Ketoconazole 79517-01-4, Sandostatin 107868-30-4, FCE 24304 131811-53-5, EM 171 131811-54-6, EM 139 131811-55-7, EM 170 131811-62-6, EM 175 134187-64-7, EM 150 134227-19-3, EM 142 134227-20-6, EM 186
(in combination therapy including antiestrogen for breast cancer and endometrial cancer)

L19 ANSWER 17 OF 19 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
ACCESSION NUMBER: 1995:228710 BIOSIS
DOCUMENT NUMBER: PREV199598243010
TITLE: In vitro 19-norandrogen synthesis by equine placenta requires the participation of aromatase.
AUTHOR(S): Moslemi, S. (1); Silberzahn, P.; Gaillard, J.-L.
CORPORATE SOURCE: (1) Lab. Biochim., Cent. Natl. Rech. Sci. URA 609, Univ. Caen, 14032 Caen France
SOURCE: Journal of Endocrinology, (1995) Vol. 144, No. 3, pp. 517-525.
ISSN: 0022-0795.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Explants of equine full-term placenta have been shown to synthesize 19-norandrogens from labelled androgens. Steroid metabolites were purified by silica-**gel** column chromatography then analysed and quantified by C-18-reverse-phase HPLC coupled to a radioactive flow detector. 19-Norandrostenedione was subsequently re-crystallized to constant specific activity, providing unequivocal evidence of its synthesis by the equine placenta. 19-Norandrostenedione synthesis appeared to be localized in the microsomal fraction. Regardless of the substrate used, formation of 19-norandrogens was far weaker than that of oestrogens; moreover, the yield of 17-oxosteroids produced was much greater than that of 17-beta-hydroxysteroids, suggesting the presence of a dehydrogenase with predominant oxidative activity. Sulphoconjugated steroids formed were less than 0.5% of total steroids. Although 19-nortestosterone could not be

generated by equine purified aromatase incubated with labelled testosterone, the synthesis of 19-norandrogens and oestrogens by equine placental explants was blocked by two specific aromatase inhibitors, 4-hydroxyandrostenedione and fadrozole. Our results provide evidence for a placental origin of at least a part of the 19-norandrogens previously identified in the blood of the pregnant mare. Furthermore, it is suggested that 19-norandrogen biosynthesis would involve the enzymatic metabolism of 19-oxygenated androgens formed by equine aromatase.

AB Explants of equine full-term placenta have been shown to synthesize 19-norandrogens from labelled androgens. Steroid metabolites were purified by silica-**gel** column chromatography then analysed and quantified by C-18-reverse-phase HPLC coupled to a radioactive flow detector. 19-Norandrostenedione was subsequently re-crystallized to. . .

RN 9039-48-9 (AROMATASE)
434-22-0 (19-NORTESTOSTERONE)
102676-47-1 (FADROZOLE)
566-48-3 (4-HYDROXYANDROSTENEDIONE)

L19 ANSWER 18 OF 19 MEDLINE
ACCESSION NUMBER: 91191863 MEDLINE
DOCUMENT NUMBER: 91191863
TITLE: Effect of estrogen inhibitors on conceptus estrogen synthesis and development in the gilt.
AUTHOR: O'Neill L A; Geisert R D; Zavy M T; Morgan G L; Wettemann R P
CORPORATE SOURCE: Department of Animal Science, Oklahoma State University, Stillwater 74078.
SOURCE: DOMESTIC ANIMAL ENDOCRINOLOGY, (1991 Jan) 8 (1) 139-53. Journal code: DO1. ISSN: 0739-7240.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199107

AB Two estrogen antagonists (keoxifene and clomiphene) and two aromatase inhibitors (LY56110 and 4-hydroxyandrostenedione, 4-OHA) were utilized to determine the role of conceptus estrogen in trophoblastic elongation and maintenance of pregnancy in the pig. Pregnant gilts were unilaterally hysterectomized on day 10.5, and infused via a uterine arterial catheter with 200 mg of keoxifene or vehicle. The remaining uterine horn was removed based on time estimated for conceptus elongation. In a second study, pregnant gilts were injected daily with 200 mg (i.m.) of clomiphene or vehicle during pregnancy (days 10-16) and hysterectomized on day 30. A third study assessed in vitro aromatase inhibition by 4-OHA and LY56110 using trophoblastic microsomes incubated with [1 beta, 2 beta-3H]-androstenedione for 6 hr. In a fourth study, in vivo inhibition of aromatase activity was determined. For this study pregnant gilts, unilaterally hysterectomized on day 10.5, received either 4-OHA, LY56110, or vehicle. Conceptus development and uterine estrogens were quantified. None of the estrogen antagonists and aromatase inhibitors interferred with conceptus elongation. Uterine protein, calcium and acid phosphatase were similar (P greater than .10) between keoxifene- and vehicle-treated gilts. Embryonic survival of clomiphene- and vehicle-treated gilts was similar (91.5 vs 87.4%). In vitro, 4-OHA and LY56110 had 50% inhibitory concentrations of 0.1 microM and 13 nM. Treatment of gilts with 4-OHA reduced total estrogens in uterine flushings by 57% (P less than .02), whereas treatment with LY56110 did not significantly lower total estrogen content in uterine flushings. Estrogen antagonists were not effective in blocking conceptus elongation and maintenance of pregnancy. Although estrogen synthesis can be inhibited in vitro, dosages of aromatase inhibitors used were not totally effective in vivo.

CT . . .
inhibitors
Blastocyst: DE, drug effects
Blastocyst: EN, enzymology
Blastocyst: PH, physiology
Calcium: AN, analysis
Clomiphene: PD, pharmacology
Dose-Response Relationship, Drug
Electrophoresis, Gel, Two-Dimensional
*Estrogen Antagonists: PD, pharmacology
*Estrogens: BI, biosynthesis
Estrogens: PH, physiology
*Fetal Development: DE, drug effects

Least-Squares Analysis

. . .

RN 26766-37-0 (LY 56110); **566-48-3 (4-hydroxy-4-androstene-3,17-dione)**; 63-05-8 (Androstenedione); 7440-70-2 (Calcium); 84449-90-1 (Raloxifene); 911-45-5 (Clomiphene)

L19 ANSWER 19 OF 19 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90251518 EMBASE
DOCUMENT NUMBER: 1990251518
TITLE: Effect of some hormonally active steroids upon the growth of LNCaP human prostate tumour cells in vitro.
AUTHOR: Iguchi T.; Fukazawa Y.; Tani N.; Sato T.; Ozawa S.; Takasugi N.; Shuin T.; Kubotal Y.; Petrow V.
CORPORATE SOURCE: Department of Biology, Yokohama City University, 22-2 Seto,Kanazawa-ku, Yokohama 236, Japan
SOURCE: Cancer Journal, (1990) 3/4 (184-191).
ISSN: 0765-7846 CODEN: CANJEI
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
028 Urology and Nephrology
LANGUAGE: English
SUMMARY LANGUAGE: French; Spanish; English

AB Conditions for the growth of LNCaP prostate cancer cells in vitro have been studied in order to develop an assay for screening steroids. Serum-free culture conditions were included to identify any effect of serum on the growth-modulating effects of added hormones. Since growth of LNCaP cells in vitro is stimulated by testosterone (T), 5.alpha.-dihydrotestosterone (DHT) and 17.beta.-estradiol (E2), assay conditions which showed a positive response to these steroids were sought. Tumour cells grew as a monolayer in plastic culture dishes in a medium containing calf serum, charcoal-stripped serum or a serum-free medium. E2 stimulated cell proliferation on collagen **gel**, but was without effect on cells cultured in the collagen **gel** or on the plastic of culture dishes. T and DHT inhibited cell proliferation in collagen **gel** or on plastic. When a serum-free medium was employed and the cells cultured on plastic; however, all 3 steroids stimulated cell proliferation with a 40-50% increase in cell numbers at equimolar concentrations. These conditions were adopted for the assay. Drug effects were evaluated by cell count. 6-Methylene-4-pregnene-3,20-dione, chlormadinone acetate, 6-methylene testosterone acetate, 4-hydroxy-4-androstene-3,17-dione, estrogens, but not their biogenetic precursors, all stimulated cellular proliferation. Diethylstilbestrol, progesterone and cholesterol were inactive. Melengestrol acetate significantly suppressed cell growth.

AB . . . culture dishes in a medium containing calf serum, charcoal-stripped serum or a serum-free medium. E2 stimulated cell proliferation on collagen **gel**, but was without effect on cells cultured in the collagen **gel** or on the plastic of culture dishes. T and DHT inhibited cell proliferation in collagen **gel** or on plastic. When a serum-free medium was employed and the cells cultured on plastic; however, all 3 steroids stimulated. . .

CT Medical Descriptors:
*prostate carcinoma
cell culture
culture medium
cytology
drug screening
growth inhibition
growth stimulation
tumor cell line
human
human cell
male
article
priority journal
collagen gel
steroid
*6 methylenetestosterone acetate: PD, pharmacology
*androgen: PD, pharmacology
*androstanolone: PD, pharmacology
*chlormadinone: PD, pharmacology
*diethylstilbestrol: PD, pharmacology

```
     *estradiol: PD, pharmacology
     *estrogen: PD, pharmacology
     *gestagen: PD, pharmacology
     *melengestrol: PD,. . .
RN.  . . methylenetestosterone acetate) 1100-17-0; (androstanolone) 521-18-6;
     (chlormadinone) 1961-77-9; (diethylstilbestrol) 30498-85-2, 56-53-1;
     (estradiol) 50-28-2; (melengestrol) 5633-18-1; (progesterone) 57-83-0;
     (testosterone) 58-22-0; (4 hydroxyandrostenedione) 566-48-3; (6
     methyleneprogesterone) 19457-57-9; (androstenediol) 28652-91-7, 521-17-5;
     (hydroxyandrostenedione) 7121-60-0

=> s penetrat? (w) (promot? or enhanc?)
L20       5112 PENETRAT? (W) (PROMOT? OR ENHANC?)

=> s l20 and l19
L21          2 L20 AND L19

=> d ti tot

L21  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2001 ACS
TI   Drug delivery systems containing ester sunscreens and penetration
     enhancers

L21  ANSWER 2 OF 2  USPATFULL
TI     Compositions and methods for enhanced drug delivery


=> log h
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                71.91     348.94

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                               -2.94      -2.94

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:18:46 ON 11 APR 2001
Connection closed by remote host

Trying 3106016892...Open

Welcome to STN International!  Enter x:x
LOGINID:ssspta1617srh
PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS, MEDLINE, USPATFULL, BIOSIS, EMBASE'
AT 13:50:20 ON 11 APR 2001
FILE 'CAPLUS' ENTERED AT 13:50:20 ON 11 APR 2001
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FILE 'MEDLINE' ENTERED AT 13:50:20 ON 11 APR 2001
FILE 'USPATFULL' ENTERED AT 13:50:20 ON 11 APR 2001
CA INDEXING COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)
FILE 'BIOSIS' ENTERED AT 13:50:20 ON 11 APR 2001
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COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                71.91     348.94

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                               -2.94      -2.94

=> file reg
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                71.91     348.94

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                   ENTRY    SESSION
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CA SUBSCRIBER PRICE -2.94 -2.94

FILE 'REGISTRY' ENTERED AT 13:50:27 ON 11 APR 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 10 APR 2001 HIGHEST RN 330783-20-5
DICTIONARY FILE UPDATES: 10 APR 2001 HIGHEST RN 330783-20-5

TSCA INFORMATION NOW CURRENT THROUGH July 8, 2000

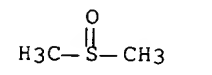
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

=> s DMSO/cn
L22 1 DMSO/CN

=> d

L22 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 67-68-5 REGISTRY
CN Methane, sulfinylbis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Methyl sulfoxide (8CI)
OTHER NAMES:
CN 15: PN: WO0068421 SEQID: 4 claimed sequence
CN Demsodrox
CN Dimethyl sulfoxide
CN Dimethyl sulphoxide
CN Dimexide
CN Dimexidum
CN Dipirartril-tropico
CN DMS 70
CN DMS 90
CN **DMSO**
CN Dolicur
CN Dromisol
CN Durasorb
CN Hyadur
CN Infiltrina
CN Somipront
CN SQ 9453
CN Sulfinylbismethane
FS 3D CONCORD
DR 8070-53-9, 164071-41-4
MF C2 H6 O S
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, APILIT, APILIT2, APIPAT, APIPAT2, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, TRCTHERMO*, TULSA, ULIDAT, USAN, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



22343 REFERENCES IN FILE CA (1967 TO DATE)
354 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
22385 REFERENCES IN FILE CAPLUS (1967 TO DATE)
39 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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=> file medline caplus embase biosis uspatfull

=> d his

     (FILE 'HOME' ENTERED AT 12:04:55 ON 11 APR 2001)

     FILE 'REGISTRY' ENTERED AT 12:05:04 ON 11 APR 2001
L1             1 S FORMESTANE/CN
L2          1477 S ANDROST-4-ENE-3,17-DIONE
L3             0 S ANDROST-4-ENE-3,17-DIONE (W) 4-ACETOXY
L4            22 S ANDROST-4-ENE-3,17-DIONE (W) 4-ACETYLOXY
L5             0 S ANDROST-4-ENE-3,17-DIONE, 4-ACETYLOXY/CN
L6               STRUCTURE UPLOADED
L7             0 S L6
L8             0 S L6 FULL
L9               STRUCTURE UPLOADED
L10            0 S L9
L11              STRUCTURE UPLOADED
L12            2 S L11
L13            0 S L11 EXA
L14            1 S L11 EXA FULL

     FILE 'CAPLUS, MEDLINE, USPATFULL, BIOSIS, EMBASE' ENTERED AT 12:58:13 ON
     11 APR 2001
L15         1414 S L1 OR L14 OR FORMESTANE
L16       203235 S TOPICAL
L17      1564492 S CREAM OR OINTMENT OR GEL OR EMULS?
L18           20 S L17 AND L15
L19           19 DUPLICATE REMOVE L18 (1 DUPLICATE REMOVED)
L20         5112 S PENETRAT? (W) (PROMOT? OR ENHANC?)
L21            2 S L20 AND L19

     FILE 'REGISTRY' ENTERED AT 13:50:27 ON 11 APR 2001
L22            1 S DMSO/CN

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS, USPATFULL' ENTERED AT 13:51:15 ON
     11 APR 2001
L23       139466 S L22 OR DMSO OR DIMETHYL SULFOXIDE

=> s l15 and l23
L24            7 L15 AND L23

=> duplicate
ENTER REMOVE, IDENTIFY, ONLY, OR (?):remove
ENTER L# LIST OR (END):123
139466 ANSWERS REQUESTED EXCEEDS MAXIMUM ALLOWED OF 50000
You may process up to 50,000 answers per command.  Please try to
narrow your search until your resulting L# answer set is within the
maximum number of answers.

=> n
N IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> duplicate
ENTER REMOVE, IDENTIFY, ONLY, OR (?):remove
ENTER L# LIST OR (END):124
PROCESSING COMPLETED FOR L24
L25            7 DUPLICATE REMOVE L24 (0 DUPLICATES REMOVED)

=> d ibib abs kwic tot

L25  ANSWER 1 OF 7  USPATFULL
ACCESSION NUMBER:         2000:80885  USPATFULL
TITLE:                    Taxanes
INVENTOR(S):              Swindell, Charles S., Merion, PA, United States
                          Shashoua, Victor E., Brookline, MA, United States
                          Bradley, Matthews O., Laytonsville, MD, United States
                          Webb, Nigel L., Bryn Mawr, PA, United States
PATENT ASSIGNEE(S):       Neuromedica, Inc., Conshohocken, PA, United States
```

(U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 6080877	20000627	
APPLICATION INFO.:	US 1997-868476	19970603	(8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1996-651429, filed on 22 May 1996, now abandoned		
DOCUMENT TYPE:	Utility		
PRIMARY EXAMINER:	Trinh, Ba K.		
LEGAL REPRESENTATIVE:	Wolf, Greenfield & Sacks, P.C.		
NUMBER OF CLAIMS:	12		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	27 Drawing Figure(s); 14 Drawing Page(s)		
LINE COUNT:	1034		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides taxanes that are conjugates of cis-docosahexaenoic acid and taxotere. The conjugates are useful in treating cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . Instructions also were provided to use the ethanol solutions containing the conjugates directly or to dissolve the analogs further in **DMSO** (dimethylsulfoxide) at appropriate concentrations, with vortexing if necessary for adequate dispersal.

DETD . . . estrogen agonists; estrogen antagonists; etanidazole; etoposide phosphate; exemestane; fadrozole; fazarabine; fenretinide; filgrastim; finasteride; flavopiridol; fiezelastine; fluasterone; fludarabine; fluorodaunorunicin hydrochloride; forfenimex; **formestane**; fostriecin; fotemustine; gadolinium texaphyrin; gallium nitrate; galocitabine; ganirelix; gelatinase inhibitors; gemcitabine; glutathione inhibitors; hepsulfam; heregulin; hexamethylene bisacetamide; hypericin; ibandronic acid;. . .

L25 ANSWER 2 OF 7 USPATFULL

ACCESSION NUMBER:	2000:7290 USPATFULL		
TITLE:	Combined use of GnRH agonist and antagonist		
INVENTOR(S):	Suzuki, Nobuhiro, Tsukuba, Japan Furuya, Shuichi, Tsukuba, Japan		
PATENT ASSIGNEE(S):	Takeda Chemical Industries, Ltd., Osaka, Japan (non-U.S. corporation)		

	NUMBER	DATE	
PATENT INFORMATION:	US 6015789	20000118	
	WO 9740846	19971106	
APPLICATION INFO.:	US 1997-894317	19970814	(8)
	WO 1997-JP1459	19970425	
		19970814	PCT 371 date
		19970814	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1996-109790	19960430
	JP 1996-138873	19960531

DOCUMENT TYPE:	Utility
PRIMARY EXAMINER:	Moezie, F. T.
LEGAL REPRESENTATIVE:	Wenderoth, Lind & Ponack, L.L.P.
NUMBER OF CLAIMS:	22
EXEMPLARY CLAIM:	1
LINE COUNT:	7339

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a pharmaceutical luteinizing hormone releasing hormone agonist in combination with a luteinizing hormone releasing hormone antagonist. By using a luteinizing hormone releasing hormone agonist and a luteinizing hormone releasing hormone antagonist in combination, the transient exacerbation with elevation of serum testosterone and estrogen owing to the pituitary-gonadotropic action (acute action) manifested immediately following an initial dose of the luteinizing hormone releasing hormone agonist can be successfully obviated.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . as tetrahydrofuran and 1,4-dioxane, aromatic hydrocarbons such

as benzene and toluene, amides such as N,N-dimethylformamide and N,N-dimethylacetamide, alkylsulfoxides such as **dimethyl sulfoxide**), in the presence of a base (e.g. alkali metal carbonate such as potassium carbonate, alkali metal hydride such as sodium. . . and 1,4-dioxane, aromatic hydrocarbons such as benzene and toluene, amides such as N,N-dimethylformamide and N,N-dimethylacetamide, and alkyl sulfoxide such as **dimethyl sulfoxide**, in the presence of a base (e.g. alkali metal carbonate such as potassium carbonate, alkali metal hydride such as sodium. . .

SUMM . . . and 1,4-dioxane, aromatic hydrocarbons such as benzene and toluene, amides such as N,N-dimethylformamide and N,N-dimethylacetamide, and alkyl sulfoxides such as **dimethyl sulfoxide**), at a temperature ranging from about 40 to 130.degree. C. in the presence of a base (e.g. alkali metal carbonate. . . and 1,4-dioxane, aromatic hydrocarbons such as benzene and toluene, amides such as N,N-dimethylformamide and N,N-dimethylacetamide, and alkyl sulfoxides such as **dimethyl sulfoxide**), in the presence of a base (e.g. alkali metal carbonate such as potassium carbonate, alkali metal hydride such as sodium. . .

SUMM . . . as tetrahydrofuran and 1,4-dioxane, aromatic hydrocarbons such as benzene and toluene, amides such as N,N-dimethylformamide and N,N-dimethylacetamide, alkylsulfoxides such as **dimethyl sulfoxide**, in the presence of a base, e.g. alkali metal carbonate such as potassium carbonate, alkali metal hydride such as sodium. . . and 1,4-dioxane, aromatic hydrocarbons such as benzene and toluene, amides such as N,N-dimethylformamide and N,N-dimethylacetamide, and alkyl sulfoxide such as **dimethyl sulfoxide**, in the presence of a base, e.g. alkali metal carbonate such as potassium carbonate, alkali metal hydride such as sodium. . .

SUMM In the reaction of the introduction of cyano group, the starting compound is dissolved in an appropriate solvent, e.g. dimethylsulfoxide (**DMSO**), and to the solution is added sodium cyanide. The reaction is carried out at 40 to 60.degree. C. for 2. . .

SUMM . . . toremifene citrate, etc.), mepitiostane, testrolactone, aminoglutethimide, droloxifene, epitiostanol, ethinylestradiol sulfonate, aromatase inhibitors (e.g. fadrozole hydrochloride, anastrozole, letrozole, Excemestane, danazol (Bonzol), **formestane**, etc.), antiandrogens (e.g. flutamide, bicalutamide, nilutamide, etc.), 5.alpha.-reductase inhibitors (e.g. finasteride, epristeride, etc.), adrenocorticoids (e.g. dexamethasone, prednisolone, betamethasone, triamcinolone, etc.),. . .

L25 ANSWER 3 OF 7 USPATFULL

ACCESSION NUMBER:	2000:4808 USPATFULL
TITLE:	Indolocarbazole derivatives useful for the treatment of neurodegenerative diseases and cancer
INVENTOR(S):	Roder, Hanno, Ratingen, Germany, Federal Republic of Lowinger, Timothy B., Nishinomiya, Japan Brittelli, David R., Branford, CT, United States VanZandt, Michael C., Guilford, CT, United States
PATENT ASSIGNEE(S):	Bayer Corporation, Pittsburgh, PA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6013646	20000111
APPLICATION INFO.:	US 1998-109131	19980702 (9)

DOCUMENT TYPE:	Utility
PRIMARY EXAMINER:	Shah, Mukund J.
ASSISTANT EXAMINER:	Kifle, Bruck
LEGAL REPRESENTATIVE:	Wolf, Greenfield & Sacks, P.C.
NUMBER OF CLAIMS:	14
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	7 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT:	1457

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel indolocarbazole derivatives potentially useful for the treatment of dementias characterized by tau hyperphosphorylation [Alzheimer's disease (AD), frontal lobe degeneration (FLD), argyrophilic grains disease, subacute sclerotizing panencephalitis (SSPE) as a late complication of viral infections in the CNS], and cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . estrogen agonists; estrogen antagonists; etanidazole; etoposide phosphate; exemestane; fadrozole; fazarabine; fenretinide; filgrastim; finasteride; flavopiridol; flezelastine; fluasterone; fludarabine; fluorodaunorunicin hydrochloride; forfenimex; **formestane**; fostriecin; fotemustine; gadolinium texaphyrin; gallium nitrate; galocitabine; ganirelix; gelatinase inhibitors; gemcitabine; glutathione inhibitors; hepsulfam; heregulin; hexamethylene bisacetamide; hypericin; ibandronic acid;. . .

DETD . . . MPLC (silica, 50-100% CH.sub.2 Cl.sub.2 -hexanes) gave the target compound (55 mg, 22-26%) as a yellow solid. .sup.1 H NMR (**DMSO**-d.sub.6) .delta. 12.19 (s, 1H), 9.19 (d, J=2.7 Hz, 1H), 9.10 (d, J=2.7 Hz, 1H), 7.78-6.87 (m, 10H), 6.81 (m, 1H),. . . by MPLC (silica, 0-15% EtOAc-CH.sub.2 Cl.sub.2) afforded the target alcohol (27 mg, 90%) as an orange powder. .sup.1 H NMR (**DMSO**-d.sub.6) .delta. 12.17 (s, 1H), 9.19 (d, J=2.6Hz, 1H), 9.10 (d, J=2.5 Hz, 1H), 7.78-6.87 (m, 10H), 6.79 (m, 1H), 6.28. . . purified by MPLC (silica, 20-30% EtOAc-hexanes) to give the cyclized product (60mg, 31%) as a yellow powder. .sup.1 H NMR (**DMSO**-d.sub.6) .delta. 9.07 (s, 1H), 9.04 (s, 1H), 8.02-6.87 (m, 10H), 6.41 (s 2H), 6.22 (m, 2H), 4.83 (s 2H), 3.68. . . flash chromatography (silica, 0-10% EtOAc-CH.sub.2 Cl.sub.2) gave the deprotected imide as an orange powder (34.9 mg, 93%). .sup.1 H NMR (**DMSO**-d.sub.6) .delta. 11.06 (s, 1H), 9.06 (s, 1H), 6.22 (d, J=2.2 Hz, 2H), 3.12 (m, 1H), 2.70 (m, 1H); MS (FAB-LSIMS). . . purified by HPLC (0-3% MeOH-chloroform) to afford the target diol as a red-orange powder (9.5 mg, 61%). .sup.1 H NMR (**DMSO** -d.sub.6) .delta. 11.05 (s, 1H), 9.05 (s, 1H), 9.02 (s, 1H), 7.85 (s, 1H), 7.65 (m, 2H), 7.39 (m, 2H), 5.51. . .

DETD . . . 25-25% CH.sub.2 Cl.sub.2 -hexanes) gave the desired mono alkylated product as an orange powder (2.0 g, 47%). .sup.1 H NMR (**DMSO**-d.sub.6) .delta. 12.13 (s, 1H), 9.21 (d, J=2.6 Hz, 1H), 9.09 (d, J=2.7 Hz), 7.77-6.87 (m, 1H), 6.07 (s, 2H), 4.79. . . by flash chromatography (silica 0-10% MeOH-EtOAc) gave the target compound as a orange-yellow solid (1.43 g, 80%). .sup.1 H NMR (**DMSO** -d.sub.6) .delta. 12.04 (s, 1H), 9.23 (d, J=2.7 Hz, 1H), 9.10 (d, J=2.7 Hz, 1H), 7.80-6.87(m, 10H), 6.11 (m, 1H), 4.81. . . by MPLC (silica, 0-20% EtOAc-CH.sub.2 Cl.sub.2) afforded the cyclized product as an orange powder (165 mg, 75%). .sup.1 H NMR (**DMSO**-d.sub.6) .delta. 9.13 (d, J=2.7 Hz, 1H), 9.08 (d, J=2.7 Hz, 1H), 8.04-6.96 (m, 10H), 5.98 (m, 1H), 5.70 (m, 1H),. . . chromatography (silica, 80-100% CH.sub.2 Cl.sub.2 -hexanes) afforded the target ketone as a yellow powder (108 mg, 77%). .sup.1 H NMR (**DMSO**-d.sub.6) .delta. 9.05 (d, J=2.6 Hz, 1H), 9.03 (d, J=2.4 Hz, 1H), 7.98-6.86 (m, 1H), 6.14 (m, 1H), 5.58 (m, 1H),. . . by flash chromatography (silica, 20% EtOAc-hexanes) provided the addition product as a yellow solid (67 mg, 26%). .sup.1 H NMR (**DMSO**-d.sub.6) .delta. 9.06 (m, 2H), 8.17-6.87 (m, 10H), 5.74 (m, 1H), 5.05 (s, 1H), 4.85 (s, 2H), 3.69 (s 3H), 3.01. . . flash chromatography (silica, 10-20% EtOAc-CH.sub.2 Cl.sub.2) afforded the target imide as a yellow solid (11.0 mg, 77%). .sup.1 H NMR (**DMSO**-d.sub.6) .delta. 11.04 (s, 1H), 9.03 (m, 2H), 7.90-7.33 (m, 6H), 5.81 (m, 1H), 5.71 (m, 1H), 5.54 (s, 1H), 3.83 (s, 3H), 3.08 (m, 2H), 2.76 (m, 1H), 1.71 (m, 1H); .sup.13 CNMR (**DMSO**-d.sub.6) .delta. 175.3 (C.dbd.O), 171 (C.dbd.O imide), 170, (C.dbd.O imide,), 142.0, 140.0, 129.7, 128.4, 126.8, 126.7, 124.4, 121.3, 121.3, 121.2, 120.4,. . .

DETD . . . chromatography (silica, 10-20% EtOAc-CH.sub.2 Cl.sub.2) to afford the methyl amide as a orange powder (3.4 mg, 61%). .sup.1 H NMR (**DMSO**-d6) .delta. 11.03 (s, 1HO, 9.04 (m, 2H), 7.94-7.32 (m, 7H), 5.81 (m, 1H), 5.59 (s, 1H), 5.41 (1H) 3.25-3.05 (m,. . .

DETD . . . substrate and inhibitor were preincubated for 5-10 min at 4.degree. C. in assay buffers containing a final concentration of 2% **DMSO** before initiating the reaction with 0.25 mM .UPSILON..sup.2 P-ATP. Samples were incubated for 30 min at 37.degree. C. and reactions. . .

DETD . . . nM, 100 nM, 300 nM, 1 mM, 3 mM and 10 mM. Compound stocks were all at 10 mM in **DMSO** and dilutions were made in **DMSO** . Cells were then treated with 1 .mu.M okadaic acid (ammonium salt; LC Laboratories, dissolved at 1 mM in **DMSO**) for 90 min. All experiments, including controls, contained a final concentration of between 0.5 and 1% **DMSO**.

L25 ANSWER 4 OF 7 USPATFULL
ACCESSION NUMBER: 1999:75671 USPATFULL
TITLE: Taxane compounds and compositions

INVENTOR(S): Bradley, Matthews O., Laytonville, MD, United States
Shashoua, Victor E., Brookline, MA, United States
Swindell, Charles S., Merion, PA, United States
Webb, Nigel L., Bryn Mawr, PA, United States
PATENT ASSIGNEE(S): Neuromedica, Inc., Conshohocken, PA, United States
(U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5919815	19990706
APPLICATION INFO.:	US 1996-653951	19960522 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Reamer, James H.
LEGAL REPRESENTATIVE: Wolf, Greenfield & Sacks, P.C.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1,4
NUMBER OF DRAWINGS: 27 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 940
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides taxanes that are conjugates of cis-docosahexaenoic acid and paclitaxel. The conjugates are useful in treating cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . Instructions also were provided to use the ethanol solutions containing the conjugates directly or to dissolve the conjugates further in **DMSO** (dimethylsulfoxide) at appropriate concentrations, with vortexing if necessary for adequate dispersal.
DETD . . . estrogen agonists; estrogen antagonists; etanidazole; etoposide phosphate; exemestane; fadrozole; fazarabine; fenretinide; filgrastim; finasteride; flavopiridol; flezelastine; fluasterone; fludarabine; fluorodaunorunicin hydrochloride; forfenimex; **formestane**; fostriecin; fotemustine; gadolinium texaphyrin; gallium nitrate; galocitabine; ganirelix; gelatinase inhibitors; gemcitabine; glutathione inhibitors; hepsulfam; heregulin; hexamethylene bisacetamide; hypericin; ibandronic acid; . . .

L25 ANSWER 5 OF 7 USPATFULL
ACCESSION NUMBER: 1998:98932 USPATFULL
TITLE: DHA-pharmaceutical agent conjugates of taxanes
INVENTOR(S): Shashoua, Victor E., Brookline, MA, United States
Swindell, Charles S., Merion, PA, United States
Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
PATENT ASSIGNEE(S): Neuromedica, Inc., Conshohocken, PA, United States
(U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5795909	19980818
APPLICATION INFO.:	US 1996-651312	19960522 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Jarvis, William R. A.
LEGAL REPRESENTATIVE: Wolf, Greenfield & Sacks, P.C.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 27 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 2451
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of cis-docosahexaenoic acid and taxanes useful in treating cell proliferative disorders. Conjugates of paclitaxel and docetaxel are preferred.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . Instructions also were provided to use the ethanol solutions containing the conjugates directly or to dissolve the analogs further in **DMSO** (dimethylsulfoxide) at appropriate concentrations, with vortexing if necessary for adequate dispersal.
DETD . . . Propionate; Cormethasone Acetate; Cortodoxone; Deflazacort; Desonide; Desoximetasone; Dexamethasone Dipropionate; Diclofenac Potassium; Diclofenac Sodium; Diflorasone Diacetate; Diflumidone Sodium; Diflunisal; Difluprednate; Diftalone; **Dimethyl Sulfoxide**; Drocinonide; Endrysone; Enlimomab; Enolicam Sodium; Epirizole; Etodolac; Etofenamate; Felbinac; Fenamole; Fenbufen;

Fenclofenac; Fenclorac; Fendosal; Fenpipalone; Fentiazac; Flazalone; Fluazacort; Flufenamic Acid;. . .

DETD . . . estrogen agonists; estrogen antagonists; etanidazole; etoposide phosphate; exemestane; fadrozole; fazarabine; fenretinide; filgrastim; fmasteride; flavopiridol; flezelastine; fluasterone; fludarabine; fluorodaunorunicin hydrochloride; forfenimex; **formestane**; fostriecin; fotemustine; gadolinium texaphyrin; gallium nitrate; galocitabine; ganirelix; gelatinase inhibitors; gemcitabine; glutathione inhibitors; hepsulfam; heregulin; hexamethylene bisacetamide; hypericin; ibandronic acid;. . .

DETD . . . flunarizine; fluocalcitriol; fluorodaunorunicin hydrochloride; fluoxetine, R-; fluoxetine, S-; fluparoxan; flupirtine; flurbiprofen axetil; flurithromycin; fluticasone propionate; flutrimazole; fluvastatin; fluvoxamine; forasartan; forfenimex; **formestane**; formoterol; formoterol, R,R-; fosfomycin; trometamol; fosinopril; fosphenytoin; fostriecin; fotemustine; gabapentin; gadobenic acid; gadobutrol; gadodiamide; gadodiamide-EOB-DTPA; gadolinium texaphyrin; gadoteric acid; gadoteridol;. . .

L25 ANSWER 6 OF 7 USPATFULL

ACCESSION NUMBER: 1998:45195 USPATFULL

TITLE: Combination for treatment of proliferative diseases

INVENTOR(S): Muller, Marcel, Allschwil, Switzerland
Geiger, Thomas, Freiburg, Germany, Federal Republic of
Altmann, Karl-Heinz, Reinach, Switzerland
Fabbro, Doriano, Arlesheim, Switzerland
Dean, Nicholas M., Encinitas, CA, United States
Monia, Brett, Carlsbad, CA, United States
Bennett, Clarence Frank, Carlsbad, CA, United States

PATENT ASSIGNEE(S): Novartis Corporation, Summit, NJ, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5744460	19980428	
APPLICATION INFO.:	US 1996-612775	19960307	(8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Robinson, Douglas W.
ASSISTANT EXAMINER: Nelson, Amy J.
LEGAL REPRESENTATIVE: Nowak, Henry P.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 2910
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to combinations of PKC-targeted (especially PKC-.alpha.-targeted) deoxyribo- and ribo-oligonucleotides and derivatives thereof with other chemotherapeutic compounds, as well as to pharmaceutical preparations and/or therapies, in relation to disease states which respond to such oligonucleotides or oligonucleotide derivatives, especially to to modulation of the activity of a regulatory protein. In particular, the invention relates to products or combinations comprising antisense oligonucleotides or oligonucleotide derivatives targeted to nucleic acids encoding human PKC and other (preferably standard) chemotherapeutics, either in fixed combination or for chronologically staggered or simultaneous administration, and the combined use of both classes of compounds, either in fixed combination or for chronologically staggered or simultaneous administration, for the treatment of proliferative diseases, especially tumor diseases, that can be treated by inhibition of PKC activity, that is, where the antisense oligonucleotides or oligonucleotide derivatives are targeted to nucleic acids encoding the regulatory protein PKC or active mutated derivatives thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . leuprolide (Lupron, Lupron Depot); anti-androgens such as flutamide (Eulexin); anti-estrogens such as tamoxifen; aromatase inhibitors such as aminogluthetimide (Cytadren), lentaron (**Formestane**, 4-hydroxy-4-androsten-3,17-dione) (see EP 0 162 510), fadrozole (5-(p-cyanophenyl)-5,6,7,8-tetrahydroimidazo [1,5-a]pyridin, see EP 0 437 415 and EP 0 165 904), letrozole. . .

SUMM . . . leuprolide (Lupron, Lupron Depot); anti-androgens such as flutamide (Eulexin); anti-estrogens such as tamoxifen; aromatase inhibitors such as aminogluthetimide (Cytadren), lentaron (**Formestane**, 4-hydroxy-4-androsten-3,17-dione) (see EP 0 162

510), fadrozole (5-(p-cyanophenyl)-5,6,7,8-tetrahydroimidazo [1,5-a]pyridin, see EP 0 437 415 and EP 0 165 904), letrozole. . .

SUMM . . . acetone, nitriles, such as acetonitrile, acid anhydrides, such as acetic anhydride, esters, such as ethyl acetate, bisalkane sulfines, such as **dimethyl sulfoxide**, nitrogen heterocycles, such as pyridine, hydrocarbons, for example lower alkanes, such as heptane, or aromatic compounds, such as benzene or. . .

IT 50-02-2, Dexamethasone 50-28-2, Estradiol, biological studies 50-44-2, 6-Mercaptopurine 50-76-0, Dactinomycin 50-91-9, 5-Fluorodeoxyuridine 51-21-8, 5-Fu 52-24-4, Triethylenethiophosphoramide 53-03-2, Prednisone 53-19-0, Mitotane 55-98-1, Busulfan 56-53-1, Diethylstilbestrol 57-22-7, Vincristine 58-22-0, Testosterone 59-05-2, Methotrexate 60-34-4D, Methylhydrazine, derivs. 68-96-2, Hydroxyprogesterone 76-43-7, Fluoxymesterone 84-65-1, Anthraquinone 125-84-8, Aminoglutethimide 147-94-4, Cytosine arabinoside 154-42-7, 6-Thioguanine 290-87-9D, S-Triazine, derivs. 302-79-4, Tretinoin 320-67-2, 5-Azacytidine 520-85-4, Medroxyprogesterone **566-48-3**, Lentaron 595-33-5, Megestrol acetate 865-21-4, Vinblastine 4291-63-8, Cladribine 4342-03-4, Dacarbazine 4891-15-0, Estracyt 9015-68-3, Asparaginase 10540-29-1, Tamoxifen 13311-84-7, Flutamide 18378-89-7, Plicamycin 18883-66-4, Streptozocin 20830-81-3, Daunorubicin 29767-20-2, Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide 51264-14-3, Amsacrine 52128-35-5, Trimetrexate 53643-48-4, Vindesine 53714-56-0, Leuprolide 53910-25-1, Pentostatin 56420-45-2, Epirubicin 58957-92-9, Idarubicin 63521-85-7, Esorubicin 65807-02-5, Goserelin 75607-67-9, Fludarabine phosphate 83150-76-9, Octreotide 102676-47-1 110942-02-4, Aldesleukin 112809-51-5 120685-11-2, N-Benzoylstaurosporine 143030-47-1 149281-19-6 149400-88-4 157168-02-0 173458-56-5 196102-76-8 196102-77-9 196102-78-0
(combinations of drugs with antisense oligonucleotides for treatment of proliferative diseases)

L25 ANSWER 7 OF 7 USPATFULL

ACCESSION NUMBER: 97:17918 USPATFULL

TITLE: Compositions and methods for enhanced drug delivery

INVENTOR(S): Hale, Ron L., Woodside, CA, United States
Lu, Amy, Los Altos, CA, United States
Solas, Dennis, San Francisco, CA, United States
Selick, Harold E., Belmont, CA, United States
Oldenburg, Kevin R., Fremont, CA, United States
Zaffaroni, Alejandro C., Atherton, CA, United States

PATENT ASSIGNEE(S): Affymax Technologies N.V., Middlesex, England (non-U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5607691	19970304
APPLICATION INFO.:	US 1995-449188	19950524 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1993-164293, filed on 9 Dec 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-77296, filed on 14 Jun 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-898219, filed on 12 Jun 1992, now abandoned And a continuation-in-part of Ser. No. US 1993-9463, filed on 27 Jan 1993, now abandoned

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Levy, Neil S.

LEGAL REPRESENTATIVE: Stevens, Lauren L.

NUMBER OF CLAIMS: 5

EXEMPLARY CLAIM: 1

LINE COUNT: 5349

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods of delivering pharmaceutical agents across membranes, including the skin layer or mucosal membranes of a patient. A pharmaceutical agent is covalently bonded to a chemical modifier, via a physiologically cleavable bond, such that the membrane transport and delivery of the agent is enhanced.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD A solution of methotrexate (233 mg, 0.512 mmol) and cerium carbonate (171 mg, 0.523 mmol) in anhydrous **DMSO** (8 ml) was sonicated and stirred at room temperature for 1.5 hours. To this reaction mixture was then added a solution of 1,2-dibromoethane (188 mg, 1 mmol) in

DMSO (2 ml). The reaction mixture was stirred at room temperature for 39 hours and concentrated in vacuo. The residue was. .

DETD . . . sec
methyl), iodide salt
theophylline-7-[4-(N,N,N-trimethylamino)-
2.4 hr
butyroyloxymethyl], bromide salt
nalidixic acid, choline ester, bromide salt
66 min
nalidixic acid 6-(N,N,N-trimethylamino)-
4.8 min
hexanoyloxymethyl ester, iodide salt
formestane-4-choline carbonate, bromide salt
26 min
melatonin-1-choline carbamate, bromide salt
15 hr
digoxin-4'"-[(O-acetyl)-betonicine ester],
1.8 min
chloride salt
betonicine-O-acetate 4-nitrophenethyl ester
6 min
digoxin-3',3",12-tris-(6-trimethylaminohexanoyl-
14 hr
oxymethyl. . .

=> s l16 and l15
L26 16 L16 AND L15

=> s l23 and l19
L27 7 L23 AND L19

=> s l27 not l25
L28 0 L27 NOT L25

=> s l14 or ((4-acetoxy or 4-acetyloxy) 4-androstene dione)
MISSING OPERATOR CETYLOXY) 4-ANDROSTEN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l14 or ((4-acetoxy or 4-acetyloxy)(w) 4-androstene dione)
4 FILES SEARCHED...
L29 46 L14 OR ((4-ACETOXY OR 4-ACETYLOXY)(W) 4-ANDROSTENE DIONE)

=> s l29 and l17
L30 1 L29 AND L17

=> d ti

L30 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
TI Medicament for preventing and/or treating a mammary carcinoma containing a steroidal aromatase inhibitor

=> s l29 and l16
L31 1 L29 AND L16

=> d ti

L31 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
TI Medicament for preventing and/or treating a mammary carcinoma containing a steroidal aromatase inhibitor

=> s topic? or derm? or skin?
L32 1556438 TOPIC? OR DERM? OR SKIN?

=> s l32 and l29
L33 5 L32 AND L29

=> dplicate
DPLICATE IS NOT A RECOGNIZED COMMAND

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The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> duplicate
ENTER REMOVE, IDENTIFY, ONLY, OR (?):remove
ENTER L# LIST OR (END):133
DUPLICATE PREFERENCE IS 'CAPLUS, BIOSIS, USPATFULL'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L33
L34           4 DUPLICATE REMOVE L33 (1 DUPLICATE REMOVED)

=> d ibib abs kwic

L34  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         1999:613668  CAPLUS
DOCUMENT NUMBER:          131:223974
TITLE:                    Medicament for preventing and/or treating a mammary
                          carcinoma containing a steroidal aromatase inhibitor
INVENTOR(S):              Schmidt, Alfred; Wieland, Heinrich
PATENT ASSIGNEE(S):       S. W. Patentverwertungs G.m.b.H., Austria
SOURCE:                   PCT Int. Appl., 24 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 9947143         A1   19990923       WO 1999-EP1374   19990303
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
             KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
             MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 943333          A1   19990922       EP 1998-104949   19980318
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     AU 9931434         A1   19991011       AU 1999-31434    19990303
     BR 9908885         A    20001121       BR 1999-8885     19990303
     EP 1063998         A1   20010103       EP 1999-913218   19990303
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.:                      EP 1998-104949   19980318
                                            WO 1999-EP1374   19990303

AB   Disclosed is the use of a steroidal aromatase inhibitor e.g. Formestane,
     for producing a medicament formulated for topical use, for
     preventing and/or treating a mammary carcinoma.  The medicament provides a
     way of avoiding the side effects assocd. with systematic use.  It is thus
     possible to carry out a primary preventative treatment or else a secondary
     preventative treatment after the appearance of a mammary carcinoma.
REFERENCE COUNT:          8
REFERENCE(S):             (2) Brodie, A; Steroids 1981, V38(6), P693 CAPLUS
                          (3) Clive, C; WO 9325548 A 1993 CAPLUS
                          (4) Mauvais-Jarvis, P; WO 8503228 A 1985 CAPLUS
                          (5) S W Patentverwertungs Ges M B H; WO 9736570 A 1997
                              CAPLUS
                          (6) Schering AG; EP 0310542 A 1989 CAPLUS
                          ALL CITATIONS AVAILABLE IN THE RE FORMAT
ST   mammary carcinoma topical steroidal aromatase inhibitor;
     Formestane topical pharmaceutical mammary carcinoma
IT   Mammary gland
        (carcinoma, inhibitors; topical steroidal aromatase inhibitor
        for preventing and/or treating mammary carcinoma)
IT   Drug delivery systems
        (emulsions; topical steroidal aromatase inhibitor for
        preventing and/or treating mammary carcinoma)
IT   Drug delivery systems
        (gels; topical steroidal aromatase inhibitor for preventing
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and/or treating mammary carcinoma)
IT Drug delivery systems
(lotions; **topical** steroidal aromatase inhibitor for preventing and/or treating mammary carcinoma)
IT Antitumor agents
(mammary gland carcinoma; **topical** steroidal aromatase inhibitor for preventing and/or treating mammary carcinoma)
IT Drug delivery systems
(ointments, creams; **topical** steroidal aromatase inhibitor for preventing and/or treating mammary carcinoma)
IT Drug delivery systems
(ointments; **topical** steroidal aromatase inhibitor for preventing and/or treating mammary carcinoma)
IT Steroids, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**topical** steroidal aromatase inhibitor for preventing and/or treating mammary carcinoma)
IT Drug delivery systems
(**topical**; **topical** steroidal aromatase inhibitor for preventing and/or treating mammary carcinoma)
IT 566-48-3, Formestane 566-48-3D, Formestane, derivs. **61630-32-8**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**topical** steroidal aromatase inhibitor for preventing and/or treating mammary carcinoma)
IT 9039-48-9, Aromatase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**topical** steroidal aromatase inhibitor for preventing and/or treating mammary carcinoma)

=> d ibib abs kwic 2-4

L34 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1986:565312 CAPLUS
DOCUMENT NUMBER: 105:165312
TITLE: Inhibition of androgen receptor binding by natural and synthetic steroids in cultured human genital **skin** fibroblasts
AUTHOR(S): Breiner, M.; Romalo, G.; Schweikert, H. U.
CORPORATE SOURCE: Med. Univ.-Poliklin., Bonn, D-5300/1, Fed. Rep. Ger.
SOURCE: Klin. Wochenschr. (1986), 64(16), 732-7
CODEN: KLWOAZ; ISSN: 0023-2173
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Examn. of the ability of natural and synthetic steroids to compete with 3H-labeled dihydrotestosterone [521-18-6] binding by androgen receptors of foreskin fibroblasts derived from men with phimosis or hypospadias revealed strong competition by androgens and some progestins with estrgoens exhibiting weak competition and aromatase [9039-48-9] inhibitors and glucocorticoids being inactive.
TI Inhibition of androgen receptor binding by natural and synthetic steroids in cultured human genital **skin** fibroblasts
IT Estrogens
Progestogens
RL: BIOL (Biological study)
(androgen receptor binding of, in fibroblast of genital **skin** of human)
IT Fibroblast
(androgen receptors of, of genital **skin** of human, steroids binding by)
IT Receptors
RL: BIOL (Biological study)
(for androgens, of fibroblasts of genital **skin** of human, steroids binding by)
IT Steroids, biological studies
RL: BIOL (Biological study)
(natural and synthetic, androgen receptor binding of, in fibroblasts of genital **skin** of human)
IT Androgens
RL: BIOL (Biological study)
(receptors for, of fibroblast of genital **skin** of human, steroids binding by)

IT Penis
(disease, hypospadias, steroid binding by androgen receptor of fibroblast of genital **skin** of human in relation to)
IT Penis
(disease, phimosis, steroid binding by androgen receptor of fibroblast of genital **skin** of human in relation to)
IT Corticosteroids, biological studies
RL: BIOL (Biological study)
(gluco-, androgen receptor binding of, in fibroblast of genital **skin** of human)
IT 50-02-2 50-23-7 50-28-2, biological studies 51-98-9 52-01-7
53-43-0 56-53-1 57-63-6 57-83-0, biological studies 58-22-0
68-96-2 71-58-9 427-51-0 521-18-6 965-93-5 968-93-4 2181-04-6
4248-66-2 6533-00-2 54024-22-5 60282-87-3 **61630-32-8**
67392-87-4 79243-67-7 96301-34-7
RL: PROC (Process)
(androgen receptor binding of, in fibroblasts of genital **skin** of human)
IT 52-39-1
RL: BIOL (Biological study)
(antagonists, androgen receptor binding of, in fibroblasts of genital **skin** of human)
IT 9039-48-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, androgen receptor binding of, in fibroblasts of genital **skin** of human)

L34 ANSWER 3 OF 4 USPATFULL
ACCESSION NUMBER: 85:10502 USPATFULL
TITLE: Suppression of premature labor by use of aromatase inhibitors
INVENTOR(S): Nathanielsz, Ithaca, NY, United States
PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., Ithaca, NY, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 4500523	19850219
APPLICATION INFO.:	US 1984-597876	19840409 (6)

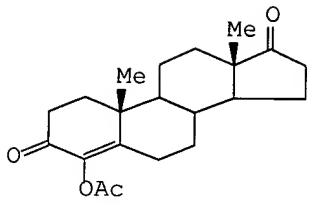
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1983-475576, filed on 15 Mar 1983, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Roberts, Elbert L.
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 317
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to the use of aromatase inhibitors to suppress premature labor in mammals by administering an aromatase inhibitor preferably 4-hydroxy-4-androstene-3,17-dione or 4-acetoxy-4-androstene-3,17-dione to a pregnant mammal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . of the rectus abdominis muscle was closed with interrupted 00 Dexon sutures. All catheters and electrodes were tunnelled under the **skin** to sites in the flank. The **skin** was closed with a subcuticular suture. After surgery the animal was placed in the restraining chair. This procedure did not. . .
IT 566-48-3 **61630-32-8**
(premature parturition suppression by)

L34 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
ACCESSION NUMBER: 1978:471306 CAPLUS
DOCUMENT NUMBER: 89:71306
TITLE: Aromatase inhibitors. III. Studies on the antifertility effect of 4-acetoxy-4-androstene-3,17-dione
AUTHOR(S): Brodie, Angela M. H.; Wu, Jung-Tsung; Marsh, David A.; Brodie, Harry J.
CORPORATE SOURCE: Worcester Found. Exp. Biol., Shrewsbury, Mass., USA
SOURCE: Biol. Reprod. (1978), 18(3), 365-70
CODEN: BIREBV; ISSN: 0006-3363
DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB 4-Acetoxy-4-androstene-3,17-dione (I) [**61630-32-8**] was an effective ovarian aromatase (estrogen synthetase) [9039-48-9] inhibitor in vitro. To study the effect of I on estrogen-dependent processes, rats were treated with silastic wafers contg. I (75 mg). These were inserted under the **skin** on day 1 of diestrus. When housed continuously with male rats from the expected day of proestrus, 7/8 rats did not mate after 6-15 days of cohabitation. Other groups of rats were treated with silastic wafers contg. I (100 mg) together with s.c. injections twice daily (12.5 mg/kg). This treatment decreased the magnitude of the proestrus estrogen surge 87% as indicated by estrogen concns. measured in ovarian vein blood. The subsequent LH [9002-67-9] surge was also inhibited over 90% as detd. by measuring peripheral levels by radioimmunoassay. None of the rats mated as long as treatment lasted (4 days). When estradiol [50-28-2] (100 .mu.g) was added to the wafers contg. I the effect on mating could be reversed and mating occurred at the normal time in 9/10 rats. Treatment of mated rats with multiple injections of I either prevented or delayed implantation. The effect was more marked at the higher dose (100 mg/kg/day). In contrast to the rat, the hamster is believed not to require estrogen for implantation. This process occurred normally in all hamsters treated with 50 mg/kg/day I and in 73% of animals treated with 100 mg/kg/day. I effectively inhibits fertility by preventing estrogen prodn. required for ovulation and implantation.

IT **61630-32-8**

RL: BIOL (Biological study)

(estrogen secretion inhibition by, contraception in relation to)